

Health Freedom Lost

Volume 2:

Regaining Health Freedom

By Thomas J. Lewis, Ph.D.

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Foreword

Foreword

"We have given up authority to central bodies of so-called experts who have agendas. The entire process is bought and paid for. If we do not take back our authority as physicians, it is all over with respect to the delivery of true health."

"I started out a gung-ho prescriber of all these drugs that I now feel are harmful"

- Richard Amerling, M.D.

The acceptance by doctors of the concept of evidence-based medicine as solely true, decided upon by a small panel of experts must be contested, and this has to be brought before the highest authority. The Supreme Court ultimately has to decide that no one really has a monopoly on the truth, especially medical truth. If we reject this notion a narrow set of experts are the only ones who can define the truth, medicine and health it lost. However, if we reject this concept and doctors can do what they are supposed to be trained to do, for the benefit of the patient, that is the essence of Hippocratic medicine. You practice for the benefit of your patient according to your best judgment and ability. You do not follow rigid guidelines. There is not a word about guidelines in the Hippocratic Oath. It is all about taking care of your patient, training others, passing on the knowledge, an iteratively improving upon what works. The Hippocratic Oath is this succinct statement of medical ethics, which we have lost? A the whole COVID fiasco has just revealed the tremendous extent to which medicine has migrated away from its core mission - to help and save lives.

There's massive over-prescribing, particularly in America, oddly where the foundation of our nation is on freedom. The model that we have adopted now is to not reverse the disease, but to rather treat those diseases with pharmaceutical products. The current system is so corrupt we have to start from scratch and build something alongside as an alternative.

Regarding the question around did we know about stopping transmission before it's entered the market? No. We had to really move at the speed of science to really understand what is taking place in the market, and from that point of view, we had to do everything at risk.

Regarding COVID and the "vaccines," We have known they showed a lack of efficacy and an inability to stop transmission from the beginning. From the first day that the initial Pfizer study was published, we knew that its effect was very limited and the conclusions were greatly overreaching. The efficacy numbers that they came up with were also not germane in the real world because they were relative risk reduction type numbers as opposed to absolute risk reduction. We knew from the beginning that the study conclusions were problematic. Also, I knew the Pfizer modus operando because they have been doing this for years with other products such as Lipitor. They never tested to stop transmission or they buried that data because it failed. The pivotal trial is the best single look that that

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drug or product will ever have because the company controls every aspect of the trial and the writing of the report.

If the treatment does not pass muster on that first trial, you know it is a bust, and that was clear from the beginning. Subsequent analyses of the study done by Bart Classen, first of all, and then Peter Doshi for the British Medical Journal, show that the number of serious adverse reactions were higher than those that were prevented by any effect of the vaccine in terms of decreasing hospitalization, or serious illness. We knew from the beginning that this was a disaster. All-cause mortality, as we now know, has gone up by an absolute value in the double digits. Shockingly, they did not start counting vaccinated until either 10 days or two weeks after the second shot, which eliminated a bunch of adverse reactions that occurred after the first shot. This is not science; it is data manipulation.

The fact that pharma did not voluntarily release the source data, and had to be forced by the court to drip it out piecemeal, with much of the information redacted, is all you need to know. They wanted to hold onto the bad news forever, 75 years is an eternity, indicates that there were serious problems with the study. They did not meet any serious endpoints and I can just imagine the mad conferences that were being conducted in that companies when those results came out and then the government did the work for them. The government was the one that said that this is going to block transmission. Pfizer never said that.

Pfizer and our governmental official did drive the coercion campaign to take the jab. The Pfizer CEO is famous for saying, "the vaccine has been proven safe and efficacious, and also I want to tell them (people reluctant to take the jab) that their decision, they need to understand, will not affect only their lives, which at the end of the day, it is their judgment, but will affect the lives of others because if they do not vaccinate, they will become the weak link that will allow this virus to replicate."

Sadly, everybody played along with it who should not have. The media, of course, ran with it as they were told to. But it was clear from the beginning that it was a false narrative and a few brave medical solders were trying to inform us but, all that stuff gets censored and it does not reach a wide audience.

Strangely, evidence-based medicine is the problem. It is actually what created the opportunity for the destruction of medicine as we knew it before. Medicine is destroyed and this is what I mean. There are several elements to its destruction.

One of the biggest and first was the loss of professional autonomy. Doctors lost control of their practices. They turned them over to corporations and large insurance companies. They stopped being able to bill directly for their services. They gave that up to the insurance industry. Many of them therefore became employees more than actual bosses of their own practice, and they had to then answer to their corporate or other bosses that were focused on profits, not care.

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This majority of doctors could not really practice unfettered medicine the way they were trained to. That was a huge thing, the loss of professional autonomy.

Then they lost their scientific roots, which is the evidence-based medicine story. This prescriptive approach that does not allow doctors to use their knowledge. And even more important, they lost their ethical mooring. Medical ethics should be forever, but instead it became changeable and fungible with every new law and passing fancy and fad. We are witness to the complete destruction of medical ethics without which you do not have a profession. You may have a trade, but you do not have a profession, and that is why I say the medical profession has been destroyed, but for a relative handful of ethical, science-based doctors out there.

One thing noted during the pandemic, is the “guidance”, which came out from the CDC or the FDA around use of drugs or around approaches to COVID in the community, effectively acted as edict, not guidance. What is evidence-based medicine? It was a construct by a couple of Canadian doctors who said we have to introduce a hierarchical system to evaluate the best evidence and then incorporate that best evidence into medical practice. It sounded good as initially devised, but something went terribly wrong.

The problem this so-called evidence system is mainly two things. One, who decides what is the best evidence? And evidence is not science. Evidence is just something that we use in a scientific process that involves thought, deductive reasoning, conscious, and rational thought. Evidence can be found to support any hypothesis but a hypothesis is a hope, not reality. Look at vitamin D in the literature, for example. There is evidence for and against it as supporting immunity. There is only one true science but many ways to create evidence.

One of the examples I love is that, according to the so-called evidence, Paul McCartney’s been dead since 1966. I do not know if you remember that whole scare, but it was a conspiracy theory that Paul died and he was substituted out and 1966 was the date and there were all these clues in their songs and you played certain things backwards on the records and you got clues. You can make up evidence or find evidence for any hypothesis, and that is not science.

Where evidence-based medicine really went sideways is when very big interests became involved in setting the guidelines. Guidance became dominated by industry, not doctors, or at least not doctors funded and supported by the pharmaceutical industry. It works this way today. The pharmaceutical industry creates the study to push their drug. They write the report to market their drug. This has all been very well-documented. We now know that the data even published in peer-reviewed journal, upon which these guidelines are based, is corrupted, so you cannot possibly use them as a way to practice medicine. Doctors, however, bought into it. It was very easy. Let’s just follow the guidelines. I can really turn my brain off at that point and just do what they say and I should do without facing liability.

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The majority of the experts are paid by industry, either as consultants, speakers, or researchers. They are getting money from industry that they are writing guidelines about. It is inherently corrupt because there are no checks and balances. Their word is final. All of these guidelines should be thrown out. We should just ignore them all. One of the things that I like to say is that if you want to be healthy, do the opposite of what the official recommendations are in terms of diet, sun, exercise, and salt. Do the opposite and you will be healthy. Eat salt, eat fat. You are going to be much healthier than if you follow the dietary guidelines.

I grew up in the 50s and 60s before these guidelines were put out, which was the end of the 70s, and everybody was slim back in those days. The obese people stood out. Now, if you are slim, you stand out. What changed? Well, our genetic makeup did not change. The dietary guidelines came out and they pushed everybody to give up animal fat go with these polyunsaturated industrially-produced vegetable oils like canola oil and soybean oil. Because they took a lot of the healthy fat out of food, it did not taste good anymore, so they amplified everything with sugar and high-fructose corn syrup, and they created a very toxic food environment that is very hard to avoid.

If you go to a supermarket, 95 percent of what is on the shelves is toxic. It is sugar-filled and soybean or canola oil-filled. You cannot even find a pretzel that does not have soybean oil anymore. You have to work very hard to eat a healthy diet in America today. The vast majority do not and they gain weight and eventually they get the metabolic syndrome, type two diabetes, hypertension, and it is all diet-related for the most part. Also, this syndrome is reversible except the model that we have adopted now is to not reverse the disease but to rather treat those diseases with pharmaceutical products that make matters worse. It is a fabulous business plan for profits.

The current system is so corrupt at this point that it is impossible to fix, in my view. We have to start from scratch and build something alongside as an alternative, because if we try to fix what is wrong, we will never finish the task. It is just so bad. We have to get all the corrupt influences out and you cannot do that as they are too entrenched. Let's just build our own system that will be free from industry influence. We are not going to have pharma telling us what drugs to give and when. We are not going to have guideline committees to tell doctors how to practice. We are going to re-instruct doctors to use real science to make clinical decisions.

Doctors have to be free to practice what they consider to be good medicine. They cannot be told how to practice. They cannot be told in California what they can discuss or not discuss with patients. There has to be free and open communication. You have to be able to give informed consent. That is another vital part in medical ethics. If you cannot tell a patient what the risks and benefits are of a given procedure, honestly, you cannot practice real medicine. You become an agent of the state, and I hope the Supreme Court has a moment of clarity and says, "No,

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you cannot assign a group to determine scientific truth,” Otherwise the current dark ages of medicine will continue.

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"Analysis of the mid-Victorian period in the U.K. reveals that life expectancy at age 5 was as good or better than exists today, and the incidence of degenerative disease was 10% of ours."

- Paul Clayton, M.D.

The Standard of Health

Summary: The mid-Victorians lived before the Flexnor report, Medicare, and the loss of health freedom by doctors in the modern era. They lacked many of the conveniences of modern society, yet most lived very healthy lives. There are important longevity lessons about how these people lived, worked, ate, and died.

Longevity is the most important way to measure the health of individuals and populations. Many presume long life implies extended misery near the end of life. Images invade our brains of breathing tubes, intravenous devices, and machines with flashing lights, all in a dreary institutional setting with the 100-year-old about to die. And, that poor unfortunate centenarian has been in that life support situation for a substantial length of time compared to someone who is about to die at the approximate global average life expectancy age of 80 years. However, the facts don't support this.

In 2013, National Geographic published their finding on a six-years study of people and populations that are very long-lived – centenarians.¹ Their findings were most interesting and illuminating. The focus was particularly on areas with unusually large numbers of people, still healthy at very ripe old ages. What they found was surprising, “genes alone are unlikely to explain all the secrets of longevity. And, in the end, genes probably account for only 25 percent of longevity. It’s the environment too, but that doesn’t explain all of it either. And don’t forget chance.” In a world of knowledge and medical advancement, is “chance” and acceptable explanation?

The Gem that emerged from this study on longevity is that people who live the longest, live the healthiest. People who live to 80, which is longer compared to the life expectancy in the United States in the 21st century, suffer 19 years of declining health. However, those who live to over 100 years of age experience only 9 years of declining health. These older people “fall off the cliff,” while those who die younger tend to slide down a slippery slope to their ultimate end. The enlightening translation of this information is 2-fold and is illustrated in Figure 1.

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Living longer – say to 100, compared to 80 years old is a 20-year difference in longevity. However, the 100-year-old people experience 30 years of extra good health. Thus, the health span of someone who lives 20 years longer is an impressive 30 years. That’s a substantial extension in good health. The improvement is 10% when considering the entire lifespan. However, it translates to a 50% improvement when starting at age 60.

Longevity and good health are linked, thus shorter life and poor health are also linked. Therefore, the measure of longevity is an objective way to measure good health.

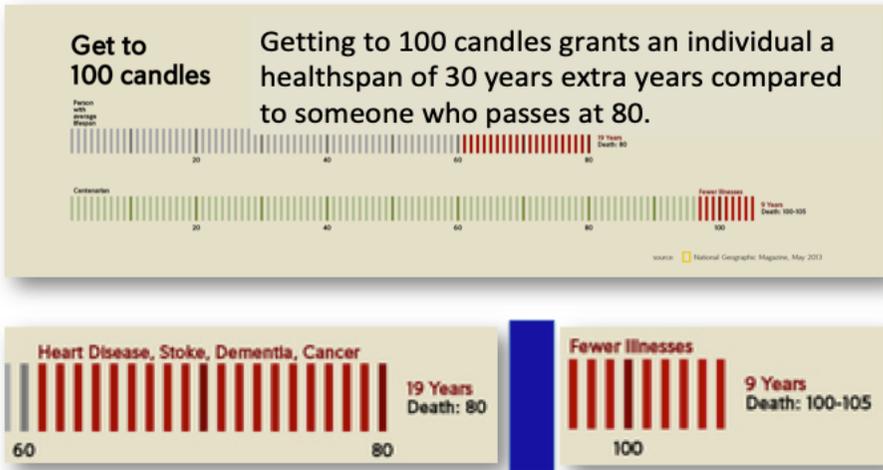


Figure 1. Lifespan and health span comparison for those who live beyond 100 years of age and those who die at age 80.

Many of the founding fathers of the United States were long-lived. According to an article titled “What the Founding Fathers Can Teach Us About Longevity,” “The first four U.S. presidents -- Washington, Adams, Jefferson and Madison -- plus Benjamin Franklin -- lived an average of more than 82 years, and they did so without the benefit of modern medical care.”² Infectious disease, which rob the life of over 40% of children below the age of six, also had an impact on mortality for those who were older, but to a lesser extent.

Hygiene and sanitation archaic in the 19th century and before based on today’s standards. Insights into the hygiene practices of the elite in society, who had the means for superior hygiene compare to regular citizens, is well documented in an article titled, “The Unique Hygiene Habits of Our Founding Fathers.”³ Poor hygiene, even today in 3rd world populations is associated with infectious diseases and early death. In the article, Thomas Paine is highlighted as one of the founding fathers who eschewed hygiene.

“Thomas Paine brought with him a history of failure when he came to America from England in 1774. As a tax collector, he was fired, rehired, and fired again

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for dereliction of duty. He failed as a maker of corsets and left two former wives behind him when he obtained a letter of introduction from Benjamin Franklin. Franklin usually exaggerated the abilities of the men he recommended for employment. In Paine's case, Old Ben merely stated his value as a, "clerk, or assistant tutor in a school". Paine's greatest service to the Revolutionary cause came from his pen, though he also served in the Continental Army in the ranks. His 1776 pamphlet *The American Crisis* opened with the memorable phrase, "These are the times that try men's souls".

Years later a friend visited Paine's apartment in Paris after the writer departed for the United States in 1802. He later wrote, "I never sat down in such a filthy apartment in the whole course of my life". He went on to describe it as "There was not a speck of cleanliness to be seen". In an earlier description of Paine's personal habits, the same writer mentioned the "brimstone odor" emitted by the writer. Another described Paine as "loathsome in appearance", always in need of bath and clean clothes, which he seldom obtained. One by one, the revolutionaries he supported, including Jefferson and Monroe, abandoned him, with multiple references to the revulsion in which he was held. Paine died in New York in 1809 at the age of 72."

The point being made by these examples is that nothing genetically has changed in the few generations where presumed life expectancy soared from 35 to 80 years.

The child mortality rate in the United States, for children under the age of five, was 462.9 deaths per thousand births in 1800. This means that for every thousand babies born in 1800, over 46 percent did not make it to their fifth birthday. Today, the death rate in this population is in the low single digits. The discovery of the vaccine affect may be considered a major cause for the reduction of early childhood mortality, thus improved longevity, but does the data corroborate this? The article "The Development of the Immunization Schedule"⁴ states,

"The next leap in vaccine recommendations and requirements for children attending schools came in 1954, when the Salk vaccine trials showed that the injected polio vaccine was highly efficacious in the prevention of paralytic polio. By 1955, the vaccine was fully licensed and Congress appropriated funds to aid local governments in buying the vaccine. By 1962, federal law further appropriated funds and directed the Centers for Disease Control and Prevention (CDC) to work with local and state health departments to deliver necessary vaccines to children as appropriate. In 1964, the Advisory Committee on Immunization Practices (ACIP) was created under the US Public Health Service to review the science and evidence of vaccines given to children and to make recommendations on when those vaccines should be given and at what age."

Antibiotics are also considered life-saving, especially for very young people who experienced very high rates of mortality due to infections. These drugs were not widely available until the 1950s. Their brief history is:

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1928: Alexander Fleming discovered the first antibiotic, penicillin. However, it took over a decade before penicillin was introduced as a treatment for bacterial infections

1930s: The first commercially available antibacterial was Prontosil, a sulfonamide developed by the German biochemist Gerhard Domagk.

1945: Penicillin was introduced on a large scale as a treatment for bacterial infections. This was possible through the work of Florey and Chain who managed to efficiently purify the antibiotic and scale-up production. The introduction of penicillin marked the beginning of the so-called “golden era” of antibiotics

1940 – 1962: The golden era of antibiotics. Most of the antibiotic classes we use as medicines today were discovered and introduced to the market.

In the article, “The Treasure Called Antibiotics,”⁵ the author, Dr. Wale Adedeji concluded,

“Prior to the beginning of the 20th Century, infectious diseases accounted for high morbidity and mortality worldwide. The average life expectancy at birth was 47 years (46 and 48 years for men and women respectively) even in the industrialized world. Infectious diseases such as smallpox, cholera, diphtheria, pneumonia, typhoid fever, plaque, tuberculosis, typhus, syphilis, etc. were rampant.”

“The antibiotic era revolutionized the treatment of infectious diseases worldwide, although with much success in developed countries. In the US for example, the leading causes of death changed from communicable diseases to non-communicable diseases (cardiovascular disease, cancer, and stroke), the average life expectancy at birth rose to 78.8 years, and older population changed from 4% to 13% of the entire US population.¹ And infectious diseases now become the problem of elderly, cancer patients, transplant patients, surgical patients, patients on immuno-suppressive drugs and other at-risk groups in developed countries.⁵ Although the developing countries also recorded a lot of improvement in the morbidity and mortality rate, infectious diseases still disproportionately affect all age group in these parts of the world.^{5,6} This is due to a combination of other factors like poverty, inadequate public health measures, poor sanitation, poor vaccination coverage, etc.”

Objective data on early childhood mortality is arguably the best information to corroborate the value of vaccines and antibiotics at saving young lives and extending life expectancy values that include children who die before the age of six. Figure 2 shows the death rate for children under five years of age in the United States.⁶

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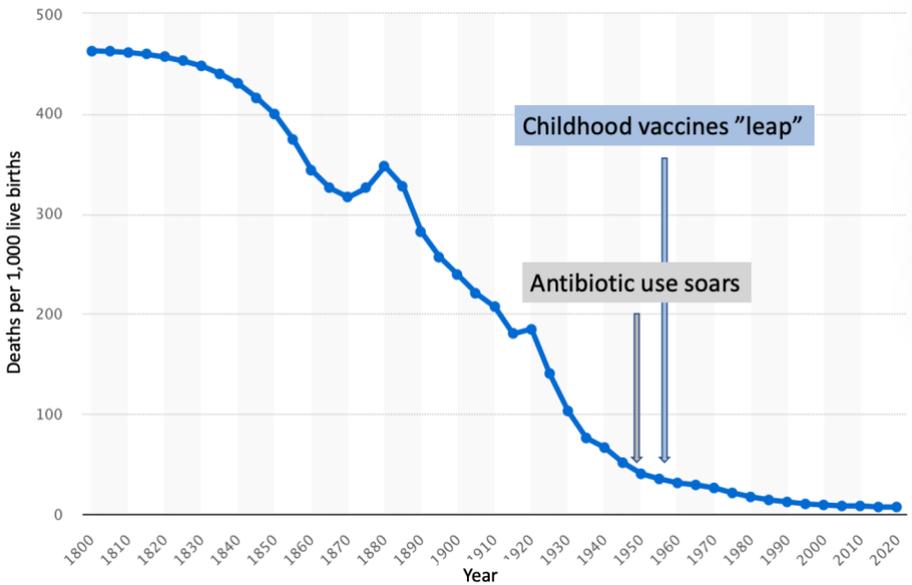


Figure 2. Death rate for children under five years of age in the United States per 1,000 live births.

The data is clear. Medicine has contributed little to longevity even in the area of early mortality caused by infectious disease. Sanitation and hygiene, as preventative measures for infectious disease played, and continues to play, the most important role at preventing premature death. In COVID-19, maintaining proper care for “barrier immunity,” that is, cleansing membranes in the mouth, nose, lungs, and gut, is mechanistically proven to reduce deaths from the disease. Biblically, human life span, as attributed to Moses, was 120 years and nothing has changed. According to various web sources in 2022, an estimated 160 – 600 people are alive who have reached the age of 110.

The medical literature contains vast references where longevity and early mortality are studied and all of them provide insight into what constitutes good health. These two concepts are important objective measures of health. The next chapter explains how these endpoints can be used to measure health and predict mortality – that is, life and health span.

The average life expectancy of the collective medical pioneers between the 16th and 19th centuries was greater than 73 years. Yet, we are told that during these times, people only lived into their 30s, or at most 40s. Why the huge disparity? Paul Clayton and Judith Rowbotham studied this conundrum and arrived at the correct answer. As it turns out, infant and early life mortality was substantial, even in the early 1900s. Thus, Clayton and Rowbotham came up with a logical way to compare longevity – by using age 5 as a starting point of comparison across time. Using this method to measure longevity – thus health – they present some startling

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information. Brits from the mid-Victorian era (~1870s) lived as long or longer when compared to Brits today.

Understanding the factors that contributed to healthy longevity back in history is relevant to what constitutes good health today. Clayton and Rowbotham published their finding in a series of four peer-reviewed papers. Their summary paper, titled, "How the mid-Victorians worked, ate and died." This paper is reproduced here with permission from the authors.

How the mid-Victorians Worked, Ate, and Died

“Analysis of the mid-Victorian period in the U.K. reveals that life expectancy at age 5 was as good or better than exists today, and the incidence of degenerative disease was 10% of ours. Their levels of physical activity and hence calorific intakes were approximately twice ours. They had relatively little access to alcohol and tobacco; and due to their correspondingly high intake of fruits, whole grains, oily fish and vegetables, they consumed levels of micro- and phytonutrients at approximately ten times the levels considered normal today. This paper relates the nutritional status of the mid-Victorians to their freedom from degenerative disease; and extrapolates recommendations for the cost-effective improvement of public health today.

The mid-Victorian period is usually defined as the years between 1850 and 1870, but in nutritional terms we have identified a slightly longer period, lasting until around 1880. During these 30 years, we argue here, a generation grew up with probably the best standards of health ever enjoyed by a modern state. The British population had risen significantly and had become increasingly urbanized, but the great public health movement had not yet been established and Britain’s towns and cities were still notoriously unhealthy environments. Despite this, and contrary to historical tradition, we argue in this paper, using a range of historical evidence, which Britain and its world-dominating empire were supported by a workforce, an army and a navy comprised of individuals who were healthier, fitter and stronger than we are today. They were almost entirely free of the degenerative diseases which maim and kill so many of us, and although it is commonly stated that this is because they all died young, the reverse is true; public records reveal that they lived as long – or longer – than we do in the 21st century.

These findings are remarkable, as this brief period of great good health predates not only the public health movement but also the great 20th century medical advances in surgery, infection control and drugs. They are also in marked contrast to popular views about Victorian squalor and disease, views that have long obscured the realities of life and death during that ‘period of equipoise’.

Our recent research indicates that the mid-Victorians’ good health was entirely due to their superior diet. This period was, nutritionally speaking, an island in time; one that was created and subsequently squandered by economic and political

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forces. This begs a series of questions. How did this brief nutritional ‘golden age’ come about? How was it lost? And could we recreate it?

One key contributory factor was what used to be called the Agricultural Revolution; a series of developments in agricultural practice that massively improved crop and livestock yields. This slow green revolution started in the late seventeenth century, gradually accelerated into the mid-19th century, and underpinned both modern urbanization and the associated Industrial Revolution. Arguably the most critical agricultural development was a more complex system of crop rotation, which greatly improved both arable output and animal husbandry.

In the 1730’s a new breed of innovative land-owner (epitomized by Marquis ‘Turnip’ Townshend) introduced new systems of crop rotation from Sweden and The Netherlands, and new crops like the swede (*Brassica napus napobrassica*). The new crop rotation systems avoided the need to let land lie fallow one year in three, and instead used a four- or five-year cycle in which turnips and clover were used as two of the crops because of their ability to replenish the soil. These new systems created immense gains in food productivity. Between 1705 and 1765 English wheat exports increased ten-fold, while the increased availability of animal feed meant that most livestock no longer had to be slaughtered at the onset of winter so that fresh (instead of salted) meat became cheaper and more widely available throughout the year.

Population shifts also played a key contributory role. The bulk of the population had always lived on the land but by 1850, as revealed by the 1851 census, more Britons were living and working in towns than in the countryside. The agricultural improvements of the previous 150 years meant that agriculture produced far more than before, but used far fewer people to achieve this. As a result, people moved to towns to find work: Britain was the first modern consumer society and there was real demand for workers in an increasing number of urban industries. Traditionally, urban life expectancy was significantly lower than rural life expectancy, but from the mid-Victorian period on this difference disappears.

Victorian society was very different to traditional society. It was a class society as we understand it today rather than the older, more deferential model, and this created enormous social tensions though it is important not to exaggerate these. For the very poor, towns remained deeply unpleasant places to live, and it can be argued that for many, the social structure of towns even got worse. As more of the working classes moved into towns, more of the middle classes moved out to create the beginnings of suburbia. The great Victorian commentator Thomas Carlyle claimed that in cities, little tied one human being to another except for the ‘Cash Nexus’, where employer and employee met in an uncomfortable wage and profit-driven relationship, as Mrs. Gaskell revealed in books like *North and South*.

In many ways, however, urban socio-economic conditions were getting better by the mid-century. Trades unions and philanthropists were slowly but surely

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improving urban working conditions and wages throughout the last half of the century. The threats of political instability which had seemed most threatening in towns up to the late 1840s were largely dispersed during the mid-Victorian era, as a result of changes in the political and legal systems. For example, the Great Reform Act of 1832 was followed by the 1867 Reform Act, which meant that most male urban heads of households were now able to vote. In 1845 the notorious Corn Laws were finally repealed ushering in the era of cheap food for the urban masses.

One of the most important results of these changes was that the interests of the landed classes were no longer protected. Traditionally, parliament had always sought to protect the income of farmers and landowners, and after the end of the Napoleonic Wars, this stance had seen the introduction of the highly unpopular Corn Laws from 1815. These kept the price of grain at a level that ensured agricultural prosperity, but they had a disastrous effect on the price of food. This particularly affected the new urban, industrial workforce, which was heavily dependent on bread as a staple food. The Corn Laws kept the price of bread artificially high, even during economic depressions such as the 1840s, a decade which became notorious as the 'Hungry 40's'.

The post-Great Reform Act parliament, however, was susceptible to pressure from groups such as the Anti-Corn Law League led by Richard Cobden and Joseph Bright. When the situation was exacerbated by the Irish Great Potato Famine, Prime Minister Sir Robert Peel, the grandson of a mill-owner, forced through the repeal of the Corn Laws. From that time on farming interests were under pressure to produce cheap food because it had become clear that the prosperity of the country depended on industrial rather than on agricultural output. As the Great Exhibition of 1851 underlined, Britain had become the Workshop of the World.

Improved agricultural output and a political climate dedicated to ensuring cheap food led to a dramatic increase in the production of affordable foodstuffs; but it was the development of the railway network that actually brought the fruits of the agricultural and political changes into the towns and cities, and made them available to the mid-Victorian working classes.

The start of the modern railway age is usually marked by the opening of the Stockton & Darlington line in 1825. From the late 1830s on, progress was impressively rapid. Important long-distance lines came first, followed by smaller local lines crisscrossing the country. The London and Birmingham line opened in 1838, part of Brunel's London to Bristol route the same year and the London and Southampton line in 1840. By the mid-century the key lines were already laid. The railway system grew exponentially, reaching 2500 miles by 1845, and continued to expand, carrying goods as well as passengers. Thanks to trains, producers were now supplying the urban markets with more, fresher and cheaper food than was previously possible. This boosted urban demand for fresh

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foodstuffs, and pushed up agricultural output still further. A survey of food availability in the 1860s through sources such as Henry Mayhew's survey of the London poor shows very substantial quantities of affordable vegetables and fruits now pouring into the urban markets.

This fortunate combination of factors produced a sea change in the nation, and in the nation's health. By 1850 Britain's increasing domestic productivity and foreign power had created a national mood of confidence and optimism which affected all levels of society. Driven by better nutrition, far more than the new schemes of clean air and water which were only beginning to have an effect from the 1870s on, adult life expectancy increased from the 1850s until by 1875 it matched or surpassed our own. The health and vitality of the British population during this period was reflected in the workforces and armed forces that powered the transformation of the urban landscape at home, and drove the great expansion of the British Empire abroad.

Unfortunately, negative changes that would undermine these nutritional gains were already taking shape. Thanks to her dominant global position, and developments in shipping technology, Britain had created a global market drawing in the products of colonial and US agriculture, to provide ever-cheaper food for the growing urban masses. From 1875 on and especially after 1885, rising imports of cheap food basics were increasingly affecting the food chain at home. Imported North American wheat and new milling techniques reduced the prices of white flour and bread. Tinned meat arrived from the Argentine, Australia and New Zealand, which was cheaper than either home-produced or refrigerated fresh meat also arriving from these sources. Canned fruit and condensed milk became widely available.

This expansion in the range of foods was advertised by most contemporaries, and by subsequent historians, as representing a significant 'improvement' in the working-class diet. The reality was very different. These changes undoubtedly increased the variety and quantity of the working-class diet, but its quality deteriorated markedly. The imported canned meats were fatty and usually 'corned' or salted.

Cheaper sugar promoted a huge increase in sugar consumption in confectionery, now mass-produced for the first time, and in the new processed foods such as sugar-laden condensed milk, and canned fruits bathed in heavy syrup. The increased sugar consumption caused such damage to the nation's teeth that by 1900 it was commonly noted that people could no longer chew tough foods and were unable to eat many vegetables, fruits and nuts. For all these reasons the late-Victorian diet actually damaged the health of the nation, and the health of the working classes in particular.

The decline was astonishingly rapid. The mid-Victorian navvies, who as seasonal workers were towards the bottom end of the economic scale, could routinely shovel up to 20 tons of earth per day from below their feet to above their heads.

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This was an enormous physical effort that required great strength, stamina and robust good health. Within two generations, however, male health nationally had deteriorated to such an extent that in 1900, five out of 10 young men volunteering for the second Boer War had to be rejected because they were so undernourished. They were not starved, but had been consuming the wrong foods. This reality is underlined by considering army recruitment earlier. The recruiting sergeants had reported no such problems during previous high-profile campaigns such as the Asante (1873-4) and Zulu (1877-8) Wars.

The fall in nutritional standards between 1880 and 1900 was so marked that the generations were visibly and progressively shrinking. In 1883 the infantry was forced to lower the minimum height for recruits from 5ft 6 inches to 5ft 3 inches. This was because most new recruits were now coming from an urban background instead of the traditional rural background (the 1881 census showed that over three-quarters of the population now lived in towns and cities). Factors such as a lack of sunlight in urban slums (which led to rickets due to Vitamin D deficiency) had already reduced the height of young male volunteers.

Lack of sunlight, however, could not have been the sole critical factor in the next height reduction, a mere 18 years later. By this time, clean air legislation had markedly improved urban sunlight levels; but unfortunately, the supposed ‘improvements’ in dietary intake resulting from imported foods had had time to take effect on the 16-18-year-old cohort. It might be expected that the infantry would be able to raise the minimum height requirement back to 5ft. 6 inches. Instead, they were forced to reduce it still further, to a mere 5ft. British officers, who were from the middle and upper classes and not yet exposed to more than the occasional treats of canned produce, were far better fed in terms of their intake of fresh foods and were now on average a full head taller than their malnourished and sickly men.

In 1904, and as a direct result of the Boer disaster, the government set up the Committee on Physical Deterioration. Its report, emphasizing the need to provide school meals for working class children, reinforced the idea that the urban working classes were not only malnourished at the start of the twentieth century but also (in an unjustified leap of the imagination, reinforced by folk memories of the ‘Hungry 40’s) that they had been so since the start of nineteenth century industrial urbanization. This profound error of thought was incorporated into subsequent models of public health, and is distorting and damaging healthcare to this day.

The crude average figures often used to depict the brevity of Victorian lives mislead because they include infant mortality, which was tragically high. If we strip out peri-natal mortality, however, and look at the life expectancy of those who survived the first five years, a very different picture emerges. Victorian contemporary sources reveal that life expectancy for adults in the mid-Victorian period was almost exactly what it is today. At 65, men could expect another ten

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years of life; and women another eight (the lower figure for women reflects the high danger of death in childbirth, mainly from causes unrelated to malnutrition). This compares surprisingly favorably with today's figures: life expectancy at birth (reflecting our improved standards of neo-natal care) averages 75.9 years (men) and 81.3 years (women); though recent work has suggested that for working class men and women this is lower, at around 72 for men and 76 for women.

If we accept the working-class figures, which are probably more directly comparable with the Victorian data, women have gained three years of life expectancy since the mid-Victorian period while men have actually fallen back by 3 years. The decline in male life expectancy implicates several causal factors; including the introduction of industrialized cigarette production in 1883, a sustained fall in the relative cost of alcohol and a severe decline in nutritional standards, as outlined below.

The improvement in female life expectancy can be partly linked to family planning developments but also to other factors promoting women's health such as improvements in dress. Until widespread accessible family planning facilities arrived after the First World War, women's health could be substantially undermined by up to 30 years of successive pregnancies and births. These figures suggest that if twentieth century women had not also experienced the negative impacts of tobacco consumption becoming respectable, along with an increased alcohol intake and worsening nutrition as they began to consume the imported delicacies originally preserved mainly for the men (all those things which had cost their menfolk three years), they would have gained six years.

Given that modern pharmaceutical, surgical, anesthetic, scanning and other diagnostic technologies were self-evidently unavailable to the mid-Victorians, their high life expectancy is very striking, and can only have been due to their health-promoting lifestyle. But the implications of this new understanding of the mid-Victorian period are rather more profound. It shows that medical advances allied to the pharmaceutical industry's output have done little more than change the manner of our dying. The Victorians died rapidly of infection and/or trauma, whereas we die slowly of degenerative disease. It reveals that with the exception of family planning, the vast edifice of twentieth century healthcare has not enabled us to live longer but has in the main merely supplied methods of suppressing the symptoms of degenerative diseases which have emerged due to our failure to maintain mid-Victorian nutritional standards. Above all, it refutes the Panglossian optimism of the contemporary anti-ageing movement whose protagonists use 1900 – a nadir in health and life expectancy trends – as their starting point to promote the idea of endlessly increasing life span. These are the equivalent of the get-rich-quick share pushers who insisted, during the dot.com boom, that we had at last escaped the constraints of normal economics. Some believed their own message of eternal growth; others used it to sell junk bonds they knew were worthless. The parallels with today's vitamin pill market are

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obvious, but this also echoes the way in which Big Pharma trumpets the arrival of each new miracle drug.

In short, the majority of even the poorest mid-Victorians lived well, despite all their disadvantages and what we would now consider discomforts. Those that survived the perils of childbirth and infancy lived as long as we do, and were healthier while they were alive their prolonged good health was due to their high levels of physical activity, and as a consequence, how and what they ate. We could learn a good deal from them.

How the Mid-Victorians Worked:

Due to the high levels of physical activity routinely undertaken by the Victorian working classes, calorific requirements ranged between 150 and 200% of today's historically low values. Almost all work involved moderate to heavy physical labor, and often included that involved in getting to work. Seasonal and other low-paid workers often had to walk up to six miles per day. While some Victorian working-class women worked from home (seam stressing for instance) more went out to work in shops, factories and workshops, necessitating long days on their feet, plus the additional burden of housework. Many single women were domestics, either live-in servants or daily workers. This was particularly physically demanding, as very few households had male servants, so women did all the heavy household work from scrubbing floors to heaving coals upstairs. Men worked on average 9-10 hours/day, for 5.5 to 6 days a week, giving a range from 50 to 60 hours of physical activity per week. Factoring in the walk to and from work increases the range of total hours of work-related physical activity up to 55 to 70 hours per week. Women's expenditure of effort was similarly large. Married women had also domestic chores in their own homes after work, and in addition, their daily dress up to the 1890s at least (when the development of the tailor-made costume reduced both corseting and the weight of numerous layers of fabric) involved real physical effort just in moving around. Male leisure activities such as gardening and informal football also involved substantial physical effort.

Using average figures for work-related calorie consumption, men required between 280 (walking) and 440 calories (heavy yard work) per hour; with women requiring between 260 and 350 calories per hour. This gives calorific expenditure ranges during the working week of between 3,000 to 4,500 calories /day (men) and 2,750 to 3,500 (women).

Total calorific requirements were likely to have been even higher during the winter months; with less insulated and less warmed homes, working class Victorians used more calories to keep warm than we do. The same held true for workplaces, unless the work (certain factory operations, blacksmithing, etc.) heated the environment to unhealthy levels. At the top end of the physical activity range were the 'navigators', the laborers who built (largely without machinery) the roads and railways that enabled the expansion of the British economy. These men were expending 5,000 calories or more per day.

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In short, the mid-Victorians ate twice as much as we do, but due to their high levels of physical activity remained slim; overweight and obesity were relatively rare, and (unless associated with ill-health) were generally identified as a phenomenon associated with the numerically smaller middle and upper-middle class. But it is not just the amount of food the mid-Victorians consumed that is so unfamiliar; the composition of their diet was also very different from our own.

What the Mid-Victorians Ate:

Onions were amongst the cheapest vegetables, widely available all year around at a cost so negligible that few housewives budgeted what cost them around a halfpenny (even cheaper if bruised) for a bunch containing at least a dozen. They might become slightly more expensive in the late spring, when leeks could be substituted. Watercress was another cheap staple in the working-class diet, available at a halfpenny for four bunches in the period April to February. The Jerusalem artichoke was consumed from September through to March, often home-grown as it was one of the easiest vegetables to grow in urban allotments. Carrots and turnips were inexpensive staples, especially during the winter months. Cabbage was also cheap and readily available, along with broccoli. Fresh peas were available and affordable from June to July, with beans from July to September.

Apples were the cheapest and most commonly available urban fruits from August through to May; with cherries taking over in the May- July period, followed by gooseberries in June, up to August, then plums and greengages in July through to September. Dried fruits and candied peel were always cheaply available, and used to sweeten desserts such as bread puddings and for cakes and mincemeat. They were also consumed as an afternoon snack, particularly by children, according to Victorian cookery books and many other sources from Dickens to Mayhew. All fruits and vegetables were organically grown, and therefore had higher levels of phytonutrients than the intensively grown crops we eat today.

Dried legumes were available all year round, and widely used (e.g. pease pudding). The chestnut was the most commonly consumed nut and one of the most commonly eaten street snacks in the chestnut season, running from September through to January. Filberts or hazelnuts were available from October through to May; walnuts were another regularly bought seasonal nut. Imported almonds and Brazil nuts were more expensive, but widely consumed around Christmas as a 'treat'. Coconuts were also imported, often given as presents or won at fairs; commonly grated for use in cakes and desserts.

The herring was one of the most important fish in the Victorian urban diet; fresh in the autumn, winter and spring; dried and salted (red herring) or pickled/soused all year round. Red herrings were a staple of the working-class diet throughout the year because they were easily cooked (e.g. *Idylls of the Poor*). Other favorites were cheap and easily obtainable varieties with better keeping qualities than the more vulnerable white fish, including sprats, eels, and shellfish (oysters, mussels,

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cockles, whelks). Of the white fish consumed, cod, haddock and John Dory were preferred. Typically, and unlike today, the whole fish was consumed including heads and roes. Fish was available from Monday evening to Friday evening; with broken and day-old fish or eels and shoreline shellfish available on Saturdays, as fishermen did not go out over the weekends.

Consumption of meat was considered a mark of a good diet and its complete absence was rare: consuming only limited amounts was a poverty diet. Joints of meat were, for the poor, likely to be an occasional treat. Yet only those with the least secure incomes and most limited housing, and so without either the cooking facilities or the funds, would be unlikely to have a weekly Sunday joint; even they might achieve that three or four times a year, cooked in a local cookhouse or bakery oven. Otherwise, meat on the bone (shin or cheek), stewed or fried, was the most economical form of meat, generally eked out with offal meats including brains, heart, sweetbreads, liver, kidneys and 'pluck', (the lungs and intestines of sheep). Pork was the most commonly consumed meat. All meats were from free-range animals.

Many East End households kept hens in their backyards, and Robert's study of Lancashire suggests similar patterns. Keeping a couple of hens could produce up to a dozen eggs per household per week. There were fears about adulteration of milk (frequently watered-down). Butter did not feature largely in the working-class diet. Dripping was a preferred substitute in the days before cheap margarine. Hard cheeses, as opposed to soft cheeses, were favored by the working classes as a regular part of their diet, partly because even when the heel of the cheese was too hard to eat, the ends could be toasted.

Beer was the most commonly consumed form of alcohol, but with an alcohol content significantly lower than today's beers. Careful reading of contemporary sources including cookery and domestic economy books suggest that the alcohol percent of beer consumed in the home was probably only 1% to 2%; often less as it was watered down, especially for consumption by women and children. In pubs, the alcohol content of beer was more regulated and generally higher, ranging from 2% to 3%. These are still weak beers, compared to today's average of around 5%. Spirits were more intermittently consumed by men and rarely by women: respectability and gin did not go together. Working class men and women seldom drank wine, except for port or sherry. A third or more of households were temperate or teetotal, partly due to the sustained efforts of the anti-alcohol movement.

Pipe smoking was widespread but intermittent amongst working class males, and a cigar or cheroot might be smoked on special occasions. Snuff had largely fallen out of favor, as had chewing tobacco. The big expansion in mass tobacco consumption by the working classes did not take place until after 1883, when industrial cigarette production was introduced. It was not until the twentieth

century that women of all classes became major consumers of tobacco, under the pressure of heavy advertising.

Some adulterants commonly used in Victorian foods were well-known to be toxic even then: lead chromate in mustard, mercury and arsenic compounds as colorants in confectionery and picrotoxin in beer all undoubtedly contributed to ill health. In contrast, modern nutritional biochemistry reveals that some of the other common ‘adulterants’ have potentially significant health benefits. The Hawthorne used to extend tea, for example, contained vaso- and cardio-protective flavonoids. The coriander in beer may have had some anthelmintic activity, and the watering down of beer and spirits was – from a health perspective – a generally good thing!

Dietary Summary

Mid-Victorian working-class men and women consumed between 50% and 100% more calories than we do, but because they were so much more physically active than we are today, overweight and obesity hardly existed at the working-class level. The working-class diet was rich in seasonal vegetables and fruits; with consumption of fruits and vegetables amounting to eight to 10 portions per day. This far exceeds the current national average of around three portions, and the government- recommended five-a-day. The mid-Victorian diet also contained significantly more nuts, legumes, whole grains and omega three fatty acids than the modern diet.

Much meat consumed was offal, which has a higher micronutrient density than the skeletal muscle we largely eat today. Prior to the introduction of margarine in the late Victorian period, dietary intakes of trans fats were very low. There were very few processed foods and therefore little hidden salt, other than in bread (Recipes suggest that significantly less salt was then added to meals. At table, salt was not usually sprinkled on a serving but piled at the side of the plate, allowing consumers to regulate consumption in a more controlled way.). The mid-Victorian diet had a lower calorific density and a higher nutrient density than ours. It had a higher content of fiber (including fermentable fiber), and a lower sodium/potassium ratio.

In short, the mid-Victorians ate a diet that was not only considerably better than our own, but also far in advance of current government recommendations. It more closely resembles the Mediterranean diet, proven in many studies to promote health and longevity; or even the ‘Paleolithic diet’ recommended by some nutritionists.

In terms of alcohol consumption, the comparisons with today are also revealing. Many contemporary reports suggest that around a fifth of Victorian working-class men might, when employed, spend up to a fifth of their income on beer. Assuming an average urban income ranging from £1 to £4 per week, and given mid-century pub prices of 3d to 8d per pint for beer, the reported expenditure would account for around 16 pints to 20 per week maximum or between three and four pints per

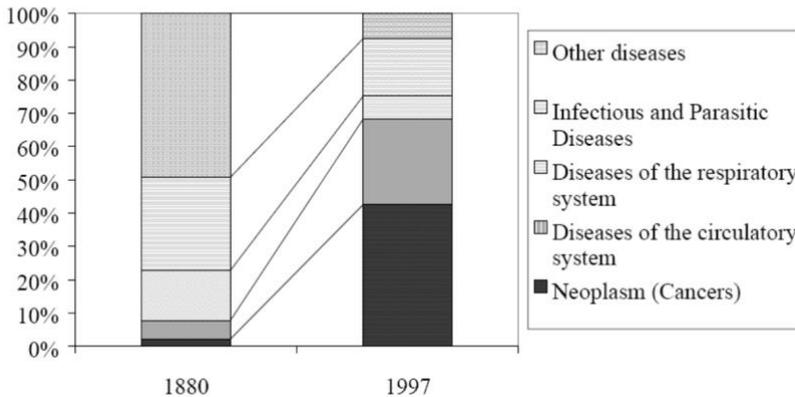
night. As Victorian beer generally had an alcohol content ranging between 1 and 3.5%, this is equivalent to one and a half to two pints of beer per day in contemporary terms. Seen in this light, the huge Victorian concerns about drunkenness in the Victorian working classes appear to be more a reflection of respectable morality than a real public health issue. Cost implications ensured that for most, the Victorian ‘alcohol problem’ was certainly less significant than it is in our time, when the frequency of public drunkenness and levels of injury and illness have become a serious public health concern (64). Finally, mid-Victorian tobacco consumption was very much lower than today.

These new findings reveal that, contrary to received wisdom, the mid-Victorians ate a healthier diet than we do today. This had dramatic effects on their health and life expectancy.

How the Mid-Victorians Died

The overall pattern of Victorian causes of death broadly resembles that found in developing countries today, with infection, trauma and infant/mother mortality in the pole positions, and non-communicable degenerative disease being relatively insignificant.

Figure 2. Causes of Death in England and Wales: 1880 and 1997. Reprinted from Charlton [24], vol. 2, p. 9.



The overall pattern of Victorian causes of death broadly resembles that found in developing countries today, with infection, trauma and infant/mother mortality in the pole positions, and non-communicable degenerative disease being relatively insignificant.

Common causes of death

Infection including TB and other lung infections such as pneumonia; epidemics (scarlet fever, smallpox, influenza, typhoid, cholera etc.), with spread often linked to poor sanitation: and the sexually transmitted diseases.

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Accidents/trauma linked to work place and domestic conditions. Death from burns was an important cause of death among women, due largely to a combination of open-hearth cooking, fashions in dress, and the use of highly flammable fabrics.

Infant/mother mortality. This was generally due to infection, although maternal hemorrhage was another significant causative factor.

Heart failure. This was generally due to damage to the heart valves caused by rheumatic fever, and was not a degenerative disease. Angina pectoris does not appear in the registrar general's records as a cause of death until 1857 – and then as a disease of old age - although the diagnosis and its causes were recognized.

Uncommon causes of death

Coronary artery disease (see above)

Paralytic fits (strokes, see Webster's Dictionary). Stroke was mainly associated with the middle and upper classes who ate a diet in which animal derived foods had a more significant role, and who consumed as a result rather less fruits and vegetables. Strokes were generally non-fatal, at least the first time; although mortality rates increased with each subsequent stroke

Cancers were relatively rare. While the Victorians did not possess sophisticated diagnostic or screening technology, they were as able to diagnose late-stage cancer as we are today; but this was an uncommon finding. In that period, cancer carried none of the stigma that it has recently acquired, and was diagnosed without bias. For example, in 1869 the Physician to Charing Cross Hospital describes lung cancer as '... one of the rarer forms of a rare disease. You may probably pass the rest of your students' life without seeing another example of it.'

Not only were cancers very uncommon compared to today, they appear to have differed in other key respects. James Paget (of Paget's Disease) built a large practice on the strength of diagnosing breast cancer, which he did by sight and palpation – that is at Stages 3 and 4. In this group he describes a life expectancy of 4 years after diagnosis, extending to eight or more with surgery. The corresponding figures today are Stage 3: 50% survival at 10 years if given surgery, chemo- and radio- therapy, and Stage 4: overall survival about 15 months. These figures suggest that breast cancer during the Victorian period was significantly less rapidly progressive than is the case today, probably due to the Victorians' significantly higher intakes of a range of micro- and phytonutrients which slow cancer growth.

In summary, although the mid-Victorians lived as long as we do, they were relatively immune to the chronic degenerative diseases that are the most important causes of ill health and death today.

What Did the Victorians Ever Do for Us?

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The implications of the mid-Victorian story are far-reaching, because, unlike the paleolithic scenario, details of the mid-Victorian lifestyle and its impact on public health are extensively documented. Thus, the mid-Victorian experience clearly shows us that:

Degenerative diseases are not caused by old age (the ‘wear and tear’ hypothesis); but are driven, in the main, by chronic malnutrition. Our low energy lifestyles leave us depleted in anabolic and anti-catabolic co-factors; and this imbalance is compounded by excessive intakes of inflammatory compounds. The current epidemic of degenerative disease is caused by widespread problem of multiple micro- and phyto-nutrient depletion (Type B malnutrition.)

With the exception of family planning and antibiotics, the vast edifice of twentieth century healthcare has generated little more than tools to suppress symptoms of the degenerative diseases which have emerged due to our failure to maintain mid-Victorian nutritional standards.

The only way to combat the adverse effects of Type B malnutrition, and to prevent and / or cure degenerative disease, is to enhance the nutrient density of the modern diet.

The Case for Supplements

Our levels of physical activity and therefore our food intakes are at an historic low. To make matters worse, when compared to the mid-Victorian diet, the modern diet is rich in processed foods. It has a higher sodium/potassium ratio, and contains far less fruit, vegetables, wholegrains and omega 3 fatty acids. It is lower in fiber and phytonutrients, in proportional and absolute terms; and, because of our high intakes of potato products, breakfast cereals, confectionery and refined baked goods, may have a higher glycemic load. Given all this, it follows that we are inevitably more likely to suffer from dysnutrition (multiple micro- and phytonutrient depletion) than our mid-Victorian forebears.

This is supported by survey findings on both sides of the Atlantic; the U.S.D.A.’s 1994 to 1996 Continuing Survey of Food Intakes by Individuals, and the National Diet and Nutrition Surveys both show that many individuals today are unable to obtain RNI values of a variety of vitamins and minerals. Malnutrition in the U.K. is now reckoned to contribute to illness-related costs in excess of £7.3 billion per annum. Since it would be unacceptable and impractical to recreate the mid-Victorian working class 4,000 calorie/day diet, this constitutes a persuasive argument for a more widespread use of food fortification and/or properly designed food supplements (most supplements on the market are incredibly badly designed; they are assembled by companies that do not understand the real nutritional issues that confront us today, and sell us pills containing irrational combinations and doses that can do more harm than good).

To insist, as orthodox nutritionists and dieticians do, that only whole fruit and veg contain the magical, health-promoting ingredients represents little more than the

last gasp of the discredited and anti-scientific theory of vitalism (‘Vitalism—the insistence that there is some big, mysterious extra ingredient in all living things—turns out to have been not a deep insight but a failure of imagination’, Daniel Dennett). Even the stately FSA concedes that fruit juices count towards your five-a-day, as do freeze-dried powdered extracts of fruits and vegetables. As our knowledge of phytochemistry and phytopharmacology increases, it has become perfectly acceptable to use rational combinations of the key plant constituents in pill or capsule form.

These arguments are developed in ‘Pharmageddon’, a medical textbook which illustrates how micro- and phyto-nutrients can be specifically combined in order to prevent and treat the chronic degenerative diseases that characterize and dominate the 20th and 21st centuries; and how they could be integrated into our food chain in order to reduce the contemporary and excessively high risks of the degenerative diseases to the far lower mid-Victorian levels.

Final Comment

In light of the huge body of evidence linking diet to health, many researchers are now studying the dietary intakes of different groups of people and attempting to tease out such esoteric factors as, for example, just how much omega 3 fish oil is necessary to reduce the risk of Alzheimer’s; or how what dose of flavonoids should be consumed to reduce the risk of stomach cancer.

Most of this research is patently a waste of time. Current generations are, from an historical point of view, anomalous. Our historically low levels of physical activity and consequently food intakes mean that even those groups consuming the highest levels of berry fruits, green leafy vegetables or oily fish, are still well below optimal (mid-Victorian) levels of consumption. For example, eminent scientists working with dietary elements thought to reduce the risk of cancer have commented that although ‘pharmacological levels’ of compounds such as flavonoids or salicylates have strong anti-cancer properties in vitro, there is little evidence that dietary (or ‘physiological’) levels of intake have any protective effects in humans.

In contrast the mid-Victorians, with their far greater intakes of fruits and vegetables, which were organic and, in many cases, contained significantly higher concentrations of phytonutrients than our intensively grown crops do were consuming ‘pharmacological’ levels of these valuable and protective compounds. This would explain why they were so effectively protected against cancer, and heart disease, and all the other degenerative, non-communicable disorders. And it would also explain why, with our very low ‘physiological’ intakes, we are so terribly prone to these largely avoidable diseases.

We believe also that the on-going search for disease susceptibility genes is ahistorical and therefore largely misinformed. The mid-Victorian gene pool was not significantly different to our own, yet their incidence of degenerative disease

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was approximately 90% less. In the high-nutrient mid-Victorian environment, the vast majority of the population was protected; and the combination of high levels of physical activity and an excellent diet enhanced the expression of a coordinated array of health-promoting genes. As the nutrient tide has receded, increasing numbers of genetic polymorphisms have become exposed, making current genome-wide association studies (GWAS) largely redundant (If we take this argument to an extreme, and progress to a diet totally devoid of micronutrients, all polymorphisms become disease-associated.). It follows that the pharmaceutical industry's attempts to develop genomically derived and individualized treatments such as RNA interference and ISPC are unlikely to impact on public health. The steel vessel of Public Health is rent open, and the drug companies are selling us high-priced pots of caulk.

Do not, therefore, look to the drug companies to provide remedies for the appalling state of our health; nor to our politicians who seem unable, in many cases, to see far beyond the brims of their parliamentary troughs. Look, instead, to the food and beverage industries, and to a lesser extent the supplement companies, who may well step up to the plate with better designed foods and nutritional programs once the currently profoundly counter-productive regulatory system has been re-drafted.”

Chapter 2. Optimal Healthspan

“He who has his stomach full, only 80% will not need a doctor.”

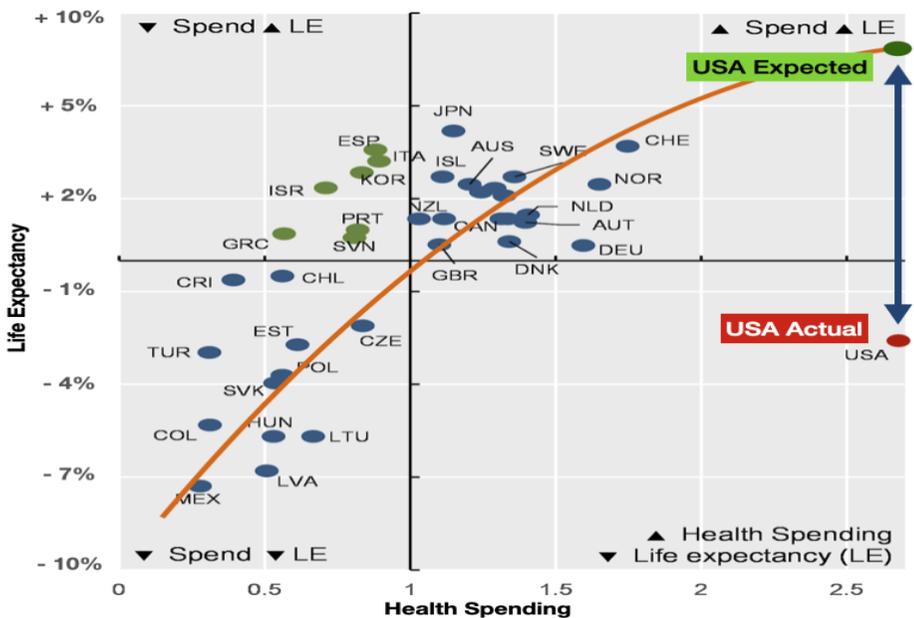
- Derived from hara hachi bu practices.

Optimal Healthspan

Americans live unhealthily compared to other developed nations, and these people continue to lose ground. Currently, the Japanese are the longest-lived nation, and the Koreans see significant gains in lifespan. Lifespan and healthspan are connected. Those who live a long life have an even longer health span when compared to their contemporaries in other countries. What the citizens of these nations do, provides insights into how we all can improve our lifespan and healthspan.

Do you want to live a long and healthy life? Most of us do. Many of us spend considerable money on testing to determine how to be healthy or regain our health. The most cost-effective way to be and stay healthy is to mimic what people do in countries that enjoy the best health and longevity.

You do NOT want to spend a lot of money on traditional healthcare. Here is a graphical representation of the Organization of Economic Cooperation and Development's (OECD) data on the 36 most developed nations' healthcare spending and longevity.



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Figure 2.1 Life expectancy (LE) versus healthcare spending in the 36 most developed nations. United States citizens spend almost 300 percent more on healthcare compared to people of the 35 other most developed nations, yet have a shorter life expectancy compared to these people.

Notice how the United States is the only outlier on the curve. The exorbitant spending is mainly due to specialization in medicine with the concomitant excesses in procedures and prescriptions that show no or even a negative benefit to longevity. The conclusion about the American health conundrum is evident, as illuminated in the figure.

The more money that you spend on healthcare, the shorter your life.

Japan (JPN) is the longest-lived nation. However, compared to Spain (ESP), citizens of Japan spend more per individual. They have a national health system that pays 70 percent of health costs while the individual is responsible for the remaining 30 percent. This 30 percent is substantial if a person is in poor health, but this approach establishes a meritocracy. In other words, 30 percent can be a minimal cost if the individual takes care of themselves. If they conduct themselves in a way that creates poor health, 30 percent is a substantial amount of money. The Japanese have a financial incentive to be healthy.

In the United States, there is no healthcare meritocracy or incentive-based system to encourage health. The financial component of the U.S. healthcare system is just the opposite and functions from the philosophy that a cured patient is a lost customer. This is surreptitiously driven by insurance companies making a percentage of the total cost. The healthcare costs associated with the poorest citizens are statistically the highest, yet their care is often heavily subsidized. These people have no monetary incentive to improve their health. And, in the case of the poor, if they are without health coverage, they use the most expensive health delivery modalities like urgent care and emergency rooms when they become sick. Seldom are these options used for routine visits. Instead, the person is in crisis mode, often requiring extreme and expensive interventions.

In no way am I inferring that the poor should be on the hook for 30 percent of their healthcare costs within the system employed in the United States. This is because the entire approach for handling this population by the government is mismanaged, extending beyond healthcare collectively has led to their poorer health. Any changes in how governments deal with this population must be re-engineered entirely to focus on the person, not their subjugation. When they have an opportunity to be healthy, mainly through dismantling and overriding the big brother approach to controlling these people, we will have a health system of meritocracy and a concomitant healthier population.

The statistics on longevity by nation are provided in Table 2.1 below. Japan is first as a nation but ranks 2nd behind the region of Hong Kong in 2021, according to the United Nations Population Division estimates. Chapter 1 explained that a

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longer life translates to a greater health span, so these statistics matter if you want to live long and well.

LE Rank	Country	LE - Average	LE - Females	LE - Males
2	Japan	85.03	88.09	81.91
4	Switzerland	84.25	86.02	82.42
5	Singapore	84.07	86.15	82.06
6	Italy	84.01	85.97	81.90
7	Spain	83.99	86.68	81.27
8	Australia	83.94	85.80	82.08
10	Iceland	83.52	84.90	82.15
11	South Korea	83.50	86.42	80.46
12	Israel	83.49	84.91	81.98
13	Sweden	83.33	84.97	81.69
46	United States	79.11	81.65	76.61

Table 2.1. Life expectancy (LE) for the longest-lived nations and the United States. Hong Kong is ranked first but is not a sovereign nation. <https://www.worldometers.info/demographics/life-expectancy/>

As you can see, the United States, with all its medical prowess, the CDC, and the FDA, lags way behind, with women experiencing 6.5 fewer years of life and men six years fewer compared to their Japanese counterparts. And, over the past several years, the life expectancy of United States citizens has declined while those of Japan and, particularly, Korea has increased. Opinions vary widely as to why the Japanese enjoy remarkable longevity. Often explanations include that the Japanese eat less red meat, for example. Is it red meat, or is it a myriad of risk factors common to those who consume lots of red meat that impact longevity? Also, have valid and unbiased studies shown that red meat is a significant causal factor? In the United States, red meat is often accompanied by French fries cooked in GMO seed oils. The chapter titled "Food! not Food?" in Volume 1 shows, without argument, that we evolved and adapted to an omnivore diet that is both animal- and plant-based. We adapted to survive and thrive, not die young.

Reductionism is a method of explaining something complex in a simplified way. However, particularly in health, this type of analysis often leads to the wrong conclusions. The antithesis of reductionism is evaluating the "many" rather than the presumed "vital few." When compared, the two board games, checkers and chess, give context to reductionism. In checkers, there are ten possible moves with

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each piece, on average. Whereas in chess, there are 30 moves. Using math no one wants to grasp called “factorial,” adding 20 moves increases possible combinations by 2×10^{18} , a number beyond the comprehension of most of us. The point of this example is that one or a couple of behavioral differences between individuals or societies does not adequately explain vast differences in health. We need to explore the myriad of behaviors that lead to good health. Your health is a chess game, not checkers. Your health is established by many things, not just the consumption of red meat or your cholesterol levels. There are substantially more significant factors than a simplified reductionist view, as exemplified by the “red meat” example.

Longevity of the Japanese - Deep Dive

I often tell people with whom I work to become a little more “Japanese” if they want to improve their health and outlook for healthy longevity. However, I never say, “Become Japanese.” As westerners, it is impossible to pick up all the cultural nuances of their society that contribute to their joy and longevity. Do you eat fermented organic soy, vegetables, and fish for breakfast? I did not think so. We must attempt to imitate their dietary style before moving on to other important aspects of their life that contribute to a longer life and health span.

Let’s have some fun with statistics to show how assumptions and what we are told can be so very wrong. The Japanese smoking rate has been consistently among the highest among males compared to men in other developed nations. A study was done on a longevity and smoking conundrum in Japan as presented in research published in 2015. The paper is titled “Association between Smoking Status and Food and Nutrient Consumption in Japanese: a Large-Scale Cross-Sectional Study.”⁷ The abstract reads, “In Japan, in comparison with the rest of the world, the death rate of lung cancer is low, although the smoking rate is relatively high. This is the so-called ‘Japanese smoking paradox.’ A healthy diet is proposed to attenuate the risk of high smoking levels. We examined the relationships between smoking status and the consumption of food and nutrients in Japan.”

Do you think the Japanese resilience to smoking is just based on the food they eat? Indeed, it plays an important role, but it is not the entire picture.

Drinking is also rampant in Japan. Figures vary widely, but the Organization for Economic Cooperation and Development puts Japan just slightly below the United States and Hungary for what are referred to as heavy drinkers but above most other developed nations, including Canada, Korea, and, surprisingly, Ireland. The point is that drinking status cannot explain the smoking conundrum.

Japan may not be a nation at the top of the published stress ladder, but its culture is typically regarded as high-stress. A recent controversy surrounding the suicide of a young worker at Japanese advertising giant, Dentsu, has cast a spotlight on the often-grueling labor conditions under which many toil in that country. It

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might come as little surprise then that many people in Japan sleep poorly because of the stress they experience at their jobs. Between 30 and 40 percent of Japanese working-age men (20-50 years old) report inadequate sleep. That is according to a recent survey about Japanese people's health and nutritional habits published by the Japanese government's Ministry of Health, Labor and Welfare.

Suicide rates are a good indication of stress. Japan is slightly below that of the United States, and these rates are double that of England. However, South Africa, Russia, and Korea are double that of Japan, yet Korea is seeing the most significant increase in life expectancy of all the developed nations.

Japan is in the upper 25 percent of the risk from smoking, drinking, and stress compared to other developed nations when taken together. Nevertheless, they are the longest-lived. Good nutrition was suggested as a reason for the "smoking paradox." Therefore, it is worth diving into this vague term of good nutrition to understand why Japanese longevity is significantly greater compared to other nations from a nutritional perspective.

Japan is a group of islands, and although there is substantial land-based agriculture in Japan, seafood consumption by the Japanese is the highest in the world. With 3 percent of the global population, this nation consumed 15 percent of the globally consumed seafood. Translated, that means the average Japanese citizen eats 500 percent more fish than the rest of the world.

Japanese citizens eat 500 percent more fish compared to the rest of the world.

When thinking about seafood consumption, the interpretation is sea flesh, that is, fish. In America, for example, a seafood meal is fried tilapia served on a GMO wheat bun from a place like Captain D's. According to the USDA, "Survey data show that while more than half of Americans meet or exceed Dietary Guidelines targets for the entire protein foods group, most people need to make changes in their choice of foods within the group to reap the health benefits of seafood and stay within limits for total calories and saturated fat. Compared to the recommended 20 percent, seafood accounted for 5 percent of total consumption from the protein foods group in 2014, which was dominated by meat and poultry."

Oh, our feds are still hung up on demonizing saturated fats. When will they read the objective literature on this topic and make healthy food recommendations?

Notice how the USDA also assumes that seafood equals sea flesh – that is, fish only. However, the sea is bountiful in other forms of seafood, that being sea vegetables. The USDA does consider two broad categories for land foods, meats and vegetables. Grains are also included in the basic recommendations by the USDA. But when it comes to the ocean, they regard only the "meat" category. They state, "Consumers also chose a relatively limited variety of seafood products. Five foods - shrimp, salmon, canned tuna, tilapia, and Alaska pollock - made up nearly three-quarters of total seafood consumption in 2014. Low-cost imports of farm-raised shrimp, salmon, and tilapia and the use of wild-caught

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Alaska pollock in fast-food fish sandwiches, frozen fish sticks, and imitation crab meat have largely driven the popularity of these four seafood species.”

Are sea vegetables even food per American regulators? It does not seem to be. In Japan, China, and Korea, they are. An article titled “Seaweed: Japan’s Underwater Superfood” by Kokoro Cares provides an excellent summary of seaweed.⁸ We need authorities from the USDA to read this. But anyone with a dim view of how government works will realize that subsidies dictate the food supply. There is no room for competition here; thus, sea vegetables will remain unacknowledged by our government.

“Seaweed has long been a staple food in Japanese diets, just as in China, Korea, and Taiwan. In recent years there has been a boom in interest in seaweed, many touting it as a “superfood,” a fact long known by Japanese people. Alongside this boom, the word “seaweed” has often been interchanged with the alternative term “sea vegetable,” which might help better capture the variety of plant or plant-like organisms known as “seaweed” that live in the oceans, rivers, and lakes throughout the world. The word “weed” is negative, at least when it comes to describing a food!

Nomenclature aside, no single term can capture the breadth and variety of seaweeds or sea vegetables that exist in our world, let alone those used in Japanese cuisine. Some might be familiar, like nori and kombu, while others might be less familiar and even a little more unusual, like umibudō and hijiki.

While there are over 10,000 species of sea vegetables or seaweeds worldwide, there are three common classifications or phyla. They are Rhodophyta, or red algae (nori); Ochrophyta, or brown algae (wakame and kombu); and Chlorophyta, or green algae (chlorella and spirulina). Among these 10,000 species of sea vegetables, nearly 1,500 can be found in the waters of Japan, 100 of which are used in Japanese cuisine, substantially more than in other countries. Each of these different seaweeds is unique and has diverse applications in Japanese cuisine, emphasizing their flexibility and versatility in the kitchen.

In Japan, people have been consuming seaweed for thousands of years. One of Japan’s earliest legal codes, the Taihō Code of 701, stated that some seaweeds (including nori, wakame, and kombu) were acceptable tax payment forms. They have long been touted for their nutritional and culinary properties, being a rich source of minerals, vitamins, fiber, and even protein (one wafer-thin 3-gram sheet of nori has the same amount of protein as one-fifth of a bottle of milk or one-fifth of an egg.) The increase in consumption of sea vegetables coincided with the spread of Buddhism in Japan, which prohibited the eating of meat. This restriction is thought to have contributed to the popularity of eating seaweed throughout Japan. Despite this rise in popularity, many forms of seaweed became readily available to the commoners living in the interior of Japan in the 17th century.

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Some evidence suggests that the Jōmon people of early Japan ate wakame as far back as 14,000 BCE. Somewhere along the line, the centuries-long custom of eating seaweed led to a “digestive evolution” in the guts of early Japanese people. Over time, bacteria from the ocean in these sea vegetables mixed with the gut bacteria of Japanese people, and in the process, began exchanging small amounts of genetic code, eventually leading to this evolution.

The Japanese people have a unique bacterial enzyme that allows them to better digest and, therefore, have better access to more of the nutrients in seaweed. Specifically, Japanese people’s guts are more readily equipped to break down the sugars and nutrients in seaweed and use it as an energy and repair source.

Sushi is wrapped in a seaweed called Nori. This may be the most frequently consumed seaweed product in the West. There are about a dozen or so prominent seaweeds, all of which confer different health benefits based on their constituents, just like broccoli has different phytonutrients and micronutrients compared to iceberg lettuce.

Some of the key benefits of sea vegetables that their land-based counterparts may not match include:

Gut health. Up to 75 percent of seaweed’s dry weight is pure fiber, which is more than most fruits and vegetables. Also, a substance in brown seaweed called alginate strengthens the gut mucus that covers the gut. Seaweed contains particular sugars called sulfated polysaccharides that help increase the growth of good bacteria and produce short-chain fatty acids that nourish the cells lining the gut.

Weight loss. People who adopt seafood and not just a sea flesh diet often report weight loss. Since seaweed is so rich in fiber, eating it can benefit those trying to shed weight. Also, a pigment in brown seaweed called fucoxanthin might reduce body fat. Scientists at Newcastle University have identified the seaweeds most effective at preventing excess fat absorption.⁹

Anti-oxidation. Many seaweeds contain antioxidant substances that naturally reduce damage from free radicals. Therefore it protects your body cells. Seaweed contains the antioxidant vitamins C and E and also flavonoids and carotenoids. Fucoxanthin, a carotenoid, protects cell membranes better than vitamin A. It has been determined to be substantially more effective as an antioxidant than vitamin D.

High nutrient density. Seaweeds are particularly concentrated in vitamins, riboflavin, and many minerals. Spirulina and chlorella types of seaweed protein have all the essential amino acids. Also, there are omega-3 fats and vitamin B12 in seaweed.

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Thyroid function. Thyroid hormones stay balanced with seaweed because they contain substantial iodine and cofactors that support iodine absorption and the reactions that synthesize the T4 and T3 hormones.

Sea Vegetables and Heart Health

Sea vegetables contain heart-healthy ingredients. No, sea vegetables are not composed of oats and other carbohydrates that the USDA claims to be heart-healthy. Instead, they contain fucoidans. According to an article in ScienceDirect,¹⁰

"Seaweed has been shown to have preventive effects on cardiovascular diseases (CVDs), such as arteriosclerosis and hypertension. Furthermore, researchers have clarified how the components contained in seaweed prevent damage to vascular endothelial cells and alleviate arteriosclerosis, dyslipidemia, and hypertension."

"In particular, fucoidan, fucoxanthin, astaxanthin, and phlorotannin have been shown to exert possible antioxidant and anti-inflammatory effects, thereby contributing to CVD prevention by protecting vascular endothelial cells. Components contained in seaweed may prevent damage to vascular endothelial cells and block the development of CVD. The protective effects of the components contained in these seaweeds against vascular endothelial dysfunction suggest that consumption of seaweed may have applications in the prevention of CVDs. There are additional studies that show that certain seaweeds serve as natural blood thinners."

"Certain seaweed pigments, particularly fucoxanthin, appear to improve insulin sensitivity. It even expressed a benefit in those with type 1 diabetes. Fucoxanthin is a specific carotenoid in brown algae and has garnered much attention for its anti-obesity and anti-diabetic effects attributable to a unique mechanism. Fucoxanthin induces uncoupling protein 1 (UCP1) expression in white adipose tissue (WAT). Furthermore, fucoxanthin improves insulin resistance and ameliorates blood glucose levels through the down-regulation of adipocytokines related to insulin resistance in WAT and the up-regulation of glucose transporter 4 (GLUT4) in skeletal muscle. Algae fucoxanthin is a beneficial compound for the prevention of metabolic syndrome. The alginates are now shown to lower the absorption of sugar into the bloodstream."

Seaweeds contain high levels of collagens of the type, which is responsible for hair recovery and even thickness. Vitamins A, C, and zinc in many types of seaweed can help with hair regrowth or prevent loss.

You are what you do not eat. If you do not eat nutritious food, you will not be healthy. Adding seaweed to traditional foods ups the levels of Micro- and phytonutrients, turning an otherwise mediocre food into one full of key nutrients.

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Consider adding seaweed to a burger or sprinkling seaweed onto any food or salad to enhance its nutritional value.

There are seven common edible varieties of seaweed. However, many Asian people consume a much greater variety.

Ogonori is also called sea moss. It has a dark purple color, and it is usually either pickled or used in salads. This food is also popular in the Caribbean and Hawaii. Ogonori is used to produce agar, a vegan-friendly counterpart of gelatin. Ogonori may be purchased in dried strips or powder and make jellies, puddings, and custards.

Kombu or brown seaweed is usually obtained in wide dry strips. The Japanese use it as a seasoning for sushi and as the main ingredient of a clear but flavorful stock called dashi. In the powdered form, it is acceptable for brewing into Japanese tea kombucha. This is the seaweed variety most attributable to good vascular health.

Nori is the most recognizable type and usually comes pressed into thin dried sheets of dark green or black color. Nori snacks are readily available at many grocery stores. It is used to make sushi rolls. Dried or toasted nori sheets can easily become soft and mushy from moisture in the air.

Wakame is a sweet seaweed with a silky texture, making it suitable for salads. It is one of the main ingredients of miso soup. Wakame is mainly sold dried and salted in vacuum packs and expands greatly during cooking.

Dulse looks like red cabbage and is unique because it tastes like bacon. It was first grown by researchers at Oregon State University in 2015. Since then, several small farms have been successfully cultivating it. The seaweed not only gets a meaty flavor when cooked but also has double the nutritional value of kale. It usually comes in the dried or holy form and sometimes in powder or seasoning mix.

Sea lettuce is dark green and leafy and frequently a constituent of soups and salads in its raw form. When cooked, it can assume a more bitter taste than when raw. An easy way to include sea lettuce into your diet is to sprinkle cut-up leaves on top of a salad or stir fry.

Umibudo, also called sea grapes, is one of the few seaweed types sold fresh. In this regard, umibudo may contain beneficial sea organisms that help digest seafood. Umibudo is composed of a long stem with tiny clusters of bubble-like leaves and is similar to caviar in texture and taste, but not cost.

Adding a small amount of highly nutritious foods like sea vegetables can counteract the adverse effects of junk foods. In a wellness program I run, I tell participants that eating something healthy has a double benefit. First, you get high nutrient density and gut-supporting fiber. Second, you do not get harmful, low-

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nutrient content from lousy food. Making a simple switch to good food or just adding some daily is the proverbial win-win.

It is time for us to realize that there is a great bounty from the sea, and it does not just include sea meats. Good health has everything to do with diversity, and in the context of good health, it means a balance of land and sea foods of all types. Following the Japanese example of consuming more sea foods and fewer land foods have the potential to increase longevity. It certainly has in Korea, Japan, and other Asian countries.

Do you think advanced AI analysis of health with tools like "Watson" will guide you to sea vegetables instead of a drug?

Sea Vegetables and Iodine

Consuming seaweed is all about consuming high levels of nutrients, not calories. Sea vegetables offer high nutrient density while offering a variety of nutrients, some of which are not in sufficient quantities in the Western diet. Iodine is one such nutrient. Iodine is NOT a trace element, and its concentration on the earth's surface, thus in foods, varies widely. Iodine is particularly concentrated in the soil and water of coastal areas.

Iodine is contained in large quantities in seaweed, fish, and seafood that are familiar to Japanese people. The "Dietary Reference Intakes for Japanese" released by the Ministry of Health, Labor, and Welfare states that the estimated average iodine requirement is 0.095 mg per day, and recommended intake is 0.13 mg per day. Most Japanese get substantially more iodine than people from other cultures due to their diet, at approximately 1 - 3 mg/day, ten times the estimated iodine daily requirement. With everything, the dose makes the poison or the cure. Concerning iodine, I do not recommend exceeding the dose that Japanese people are known to intake.

What is the actual amount of iodine consumed in Japan? An article titled "Assessment of Japanese iodine intake based on seaweed consumption in Japan: A literature-based analysis"¹¹ clarifies an important issue concerning iodine intake in Japan. The amount of iodine the Japanese consume daily from seaweeds has previously been estimated as high as 13.5 to 45 mg/day by sources that use ambiguous data to approximate intake, an amount 4.5 to 15 times greater than the safe upper limit of 3 mg/day set by the Ministry of Health, Labor and Welfare in Japan.

"While high iodine intake from seaweed consumption is believed to have numerous health benefits, it has been reported to negatively affect individuals with underlying thyroid disorders. To prevent excessive consumption, it is imperative for people seeking health benefits from a high-iodine diet to be knowledgeable of the amount of iodine the Japanese consume daily. In this paper, we use a combination of dietary records, food

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surveys, urine iodine analysis, and seaweed iodine content to provide a reliable estimate of Japanese iodine intake, primarily from seaweeds."

When a person consumes more iodine than required, the thyroid retains and stores a supply of iodine. Any excess iodine newly ingested is only partially taken into the thyroid, and most of it is excreted in the urine.

In the early 20th century, endemic iodine deficiency was prevalent in the Midwest and Western regions of the U.S., a geographic area known as the "goiter belt," where most children had a clinically apparent goiter. This problem was so severe that initial salt iodization began locally in 1924, and shortly after that, iodized salt was distributed nationally. A 2017 study found that introducing iodized salt in 1924 raised the IQ of one-quarter of the population most deficient in iodine.¹²

Iodine is most well-known in human health for producing the thyroid hormones thyroxine (T4) and triiodothyronine (T3), which play key roles in metabolic processes. The number after the "T" stands for the number of iodine atoms in the thyroid-based molecules. The major concerns regarding the global burden of iodine deficiency are related to goiter, neurocognitive impairments, and in severe deficiency, hypothyroidism resulting in cretinism.

Iodine is a critically essential nutrient. An article titled "Thyroid hormones, iodine, and the brain—an important concern,"¹³ warns about iodine deficiency. Key excerpts from this paper are reproduced here.

"Thyroid hormones are important regulators of brain development, and exposure to insufficient levels of these hormones for more than short periods of time during fetal development can lead to irreversible brain damage. The only source of thyroid hormones available to the fetus during the first trimester of pregnancy is derived from the mother; however, fetal production of thyroid hormones becomes increasingly important during the second half of pregnancy. Therefore, thyroid function should be optimal in pregnant women and their offspring if adverse effects on brain development are to be avoided."

"Thyroid deficiency falls into three key categories, each of which represents a different area of concern:

- thyroid insufficiency caused by low iodine intake (of the mother and the child);
- primary maternal thyroid insufficiency with a higher-than-normal serum TSH concentration; and
- isolated low free T4 levels in the mother."

"Severe iodine deficiency—defined as a median, population based urinary iodine concentration <20 µg/l—is associated with impairments in brain development that range from frank cretinism with multiple defects of the central nervous system to a lower than anticipated intelligence quotient.

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Some studies have indicated that moderate iodine deficiency (median urinary iodine concentrations 20–49 µg/l) might also increase the risk of impaired brain development in some individuals."

A more extensive evaluation of the importance of iodine is provided in a later chapter.

Capillary Health

Many variables explain the longevity of the Japanese. However, at the root, these variables are most likely their contributions to the health of the glycocalyx, which is the structure that supports the health of our capillaries. Critical nutrient variables that support this structure are found in seaweed and are one of many constituents that provide a vascular benefit.

Fucoidan was first found in brown seaweed algae in 1913. It is a polysaccharide containing L-fructose and sulfate moieties. It can be found in several marine sources, including sea cucumbers and brown seaweed. Since its first discovery and isolation, studies have shown that fucoidan has:

- anti-tumor,
- anti-coagulant and,
- anti-oxidant activities, as well as the
- regulating the metabolism of glucose.

Other published benefits of fucoidan intake include protection against liver damage and urinary system failures.

The most fundamental action of fucoidan on health is stabilizing the capillary bed called the glycocalyx. Understanding and maintaining the health of this capillary bed may be the third most important way to ensure healthy longevity after eating and digesting well. After all, you are what you absorb.

The endothelium is a single layer of cells that line the interior surface of blood vessels and lymphatic vessels. The endothelium forms an interface between circulating blood or lymph in the lumen, the blood vessels' interior space, and the vessel wall. Endothelial cells form the barrier between vessels and tissue and control the flow of substances and fluid into and out of a tissue. Cholesterol is an indispensable constituent of cellular membranes and plays a critical role in membrane permeability and fluidity.¹⁴ NEVER artificially lower your total cholesterol or LDL.

This vascular endothelial glycocalyx is a dense, bush-like micro-structure that is synthesized and secreted by endothelial cells and is evenly distributed on the surface of vascular endothelial cells (blood vessels). Figure 2.2.

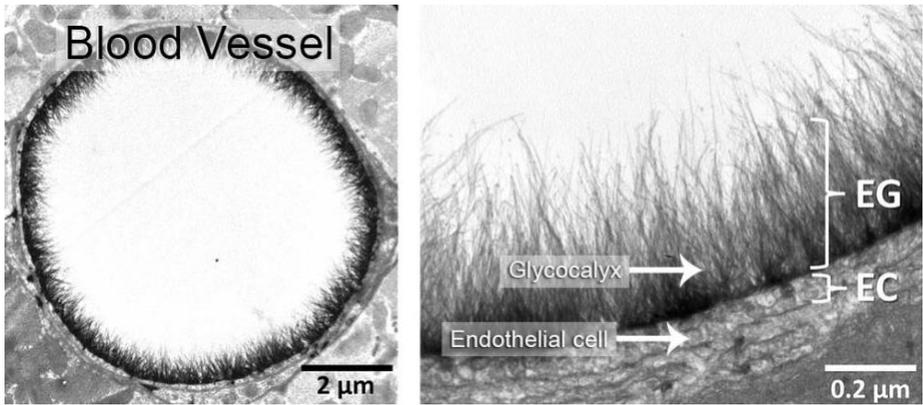
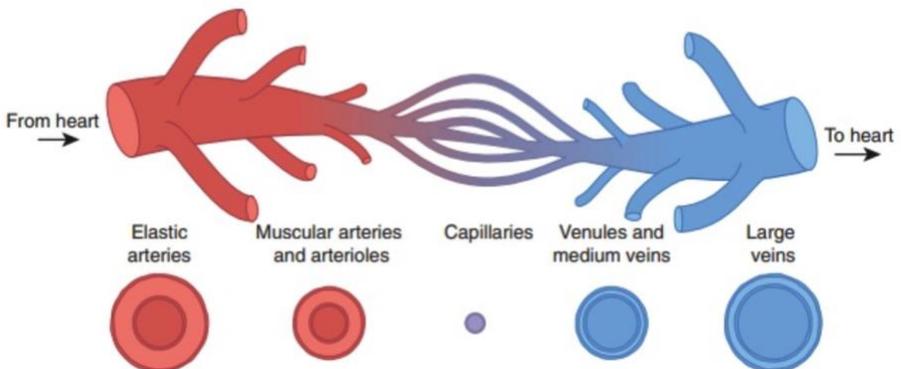


Figure 2.2. Magnified image of capillary vessels with a focus on the glycocalyx. The hair-like structures of the glycocalyx keep the blood flowing smoothly through these narrow vessels.

Knowing how your vascular system works, that is, where most of the physiological action occurs, helps define what aspects of that system are most important in determining your health. To explain where the action is in your vascular system, consider this analogy. You are going to a meeting. You get into your car, enter the freeway, and get to the designated location.

Freeway = large vessels.

While on the freeway, you are focused on arriving at the meeting site. There is very little activity going on other than driving to get to your destination. You rapidly pass by landmarks but are not interacting with them. You do NOT jump out of your car to enter the meeting at sixty miles per hour. The same is true of blood constituents coursing through the larger vessels. There is no real interaction with tissue - just movement. Red blood cells are not delivering oxygen and nutrients or picking up waste while in motion. They are just traveling to their destination. The cells are scooting along at approximately 3 feet per second within the elastic arteries, muscular arteries, and arterioles, Figure 2.3.



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Figure 2.3. Large vessels (elastic arteries) branch out to smaller vessels and eventually into capillaries. It is at the junction between the arterial (oxygen-carrying) capillaries and venous (deoxygenated) capillaries that all the physiological action occurs.

Once you leave the highway, you will get on smaller and smaller roads until you finally arrive at the meeting location. This is where the action begins. You arrive at the meeting room and sit with the other participants.

Meeting room = capillary bed.

Within the capillary bed, the blood comes to a complete stop, the red blood cells dump their oxygen cargo, and the plasma delivers nutrients and picks up waste. This does NOT happen in the larger vessels where blood is flowing quickly and continuously, Figure 2.4.

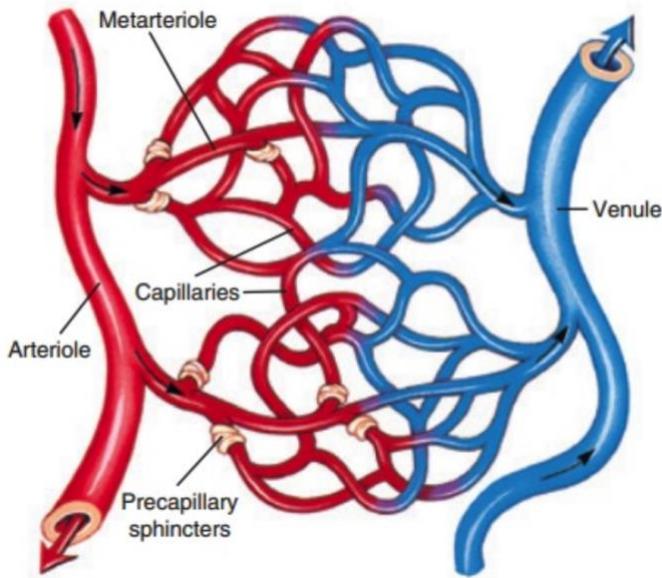


Figure 2.4. Close-up of the vascular capillary bed and the small vessels delivering blood to this region. The red vessels are oxygen-carrying arterial blood vessels, while the blue vessels are venous deoxygenated blood-carrying vessels.

The integrity of this capillary bed, the glycocalyx, is critical to health. You might ask a logical question, "I thought heart disease is of the large vessels of the heart or other large vessels?" Indeed, that is what we have been led to believe. However, a German pathologist by the name of Koester showed the following in 1876.¹⁵

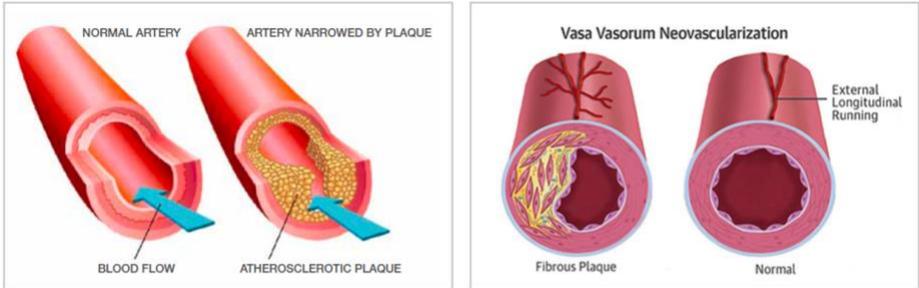
The disease of the large vessels is actually a disease of the small vessels (capillaries) supporting the large vessels.

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Another way to state this is that diseases of the large vessels start from the outside, in a region referred to as the vasa vasorum. It is in this tissue that the capillary bed (glycocalyx) resides.

This means two things:

1. To understand and optimize cardiovascular health, you must understand what makes the glycocalyx healthy.
2. The vessel diagram showing blood vessels and their clogging proudly displayed in every doctor's office is entirely wrong, Figure 2.5.



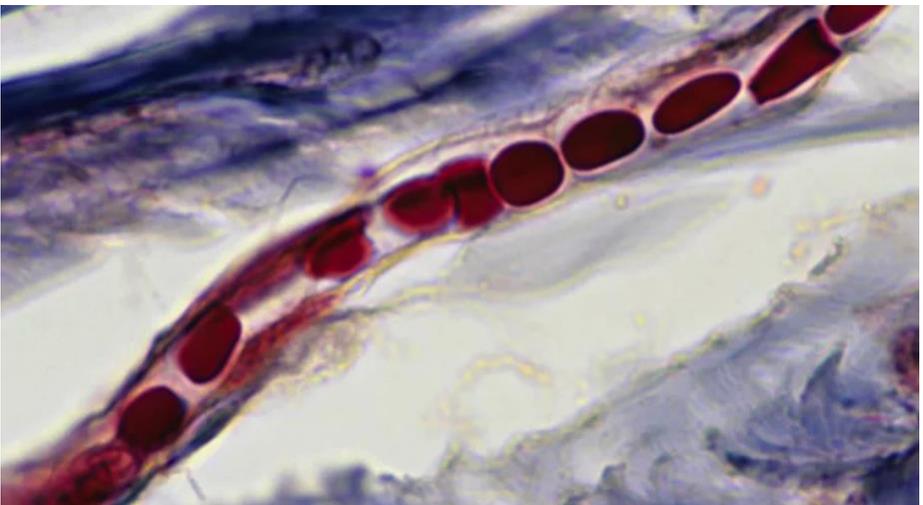
Wrong: Plaque building up from the inside

Correct: Plaque building up from the outside

Figure 2.5. Models for atherosclerosis. Left images, incorrect depiction of how plaque forms inside a large vessel. Right images, correct depiction of the heart disease, and general vessel disease process. The disease of the large vessel initiates from outside in the capillary bed of the vasa vasorum.

If your doctor has the image on the left proudly displayed in their office - run!

Red blood cells traveling through capillaries can be photographic in the eye because of the transparency of eye tissue, Figure 2.6.



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Figure 2.6. Red blood cells travel single-file through a capillary. In some instances, the red blood cells are touching each other. Some of the normal red blood cells are elongated as the inside diameter of a capillary is often smaller compared to the diameter of a red blood cell.

In many instances, blood flow through the capillary region is impeded or slowed, like a crowd trying to get into a building through a turnstile. If enough capillaries have some type of impediment to their flow, blood pressure may elevate. The dynamics of this process are multifactorial. However, one process is worth noting here because it is easily measured and, if not optimal, can be improved through readily available natural interventions. The erythrocyte sedimentation rate (ESR) is possibly the best physiological marker for poor blood flow through the capillaries. As the ESR value increases, the stickiness of red blood cells to each other also increases. At some level of ESR, structures are referred to as being in the rouleaux form, Figure 2.7.

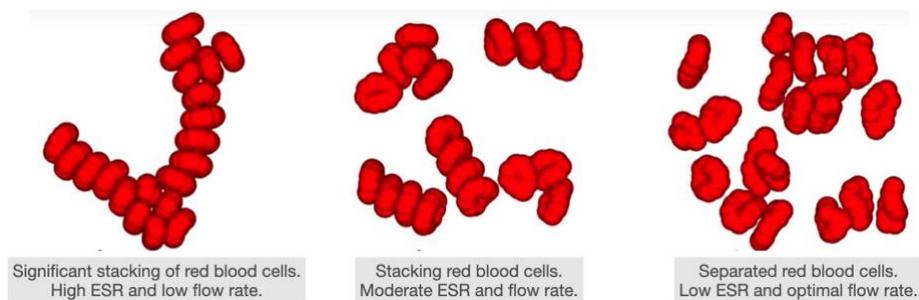


Figure 2.7. Stacking of red blood cells into formations called "rouleaux." The larger these stacks, the more force is needed to drive the blood cells through the capillaries. The erythrocyte sedimentation rate is a measure of the degree of rouleaux formation.

The images in the figures above reveal some important things about the health of red blood cells.

- Not all red blood cells are the same size. This is measured with a biomarker called the red blood cell distribution width (RDW).
- Not all red blood cells are the same shape. Larger red blood cells must elongate to squeeze through capillaries.
- Upon close examination, you can see the "hairs" of the glycocalyx extending into the capillary region. The density of these structures is correlated to the health of the capillaries.
- Some red blood cells are touching the capillary lining (glycocalyx), while others are not.
- Some red blood cells are touching each other, while some are separated. This phenomenon is best measured with the blood test erythrocyte sedimentation rate.

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- Stacked red blood cells, called rouleaux, occur when the red blood cells are sticky. This impedes blood flow or increases blood pressure.

The Glycocalyx is the gel-like lining of the capillaries and all other blood vessels. Its integrity is essential to the healthy function of all cells, organs, and body systems. This lining protects the inside walls of the capillaries and enables the transfer of nutrients and waste removal from vital organs.

The gel-like substance that is glycocalyx is a free-form matrix made up of starches, fluid, ions, and other transient substances and nutrients. An example of a free-form matrix familiar to most people is gelatin desserts made of starch and pectin. Glycocalyx may act as glue between cells and sealant between blood vessels' interior and exterior layers and capillaries. It protects surface cells and the lining of blood vessels and organs. The stickiness allows cellular interactions between the white blood cells and the protein receptors in the cell membranes.

Over time, the glycocalyx wears down and develops gaps or holes inhibiting function. This happens because of aging, poor diet, lack of exercise, genetics, stress, smoking, infection, and conditions such as diabetes and high blood pressure. Nutrient delivery and waste removal falter as the glycocalyx deteriorate. Organs suffer and starve. This manifests as localized hypoxia and, as this process further develops, vascular diseases and various downstream associated conditions. This process of glycocalyx deterioration is not felt as a specific symptom. Instead, it is at the core of most chronic diseases. Refer to Volume 1, which discusses the concept of localized focal disease.

In COVID-19, the glycocalyx suffered in many people. This is assumed, rather than measured, based on the high incidence of myocarditis and other vascular issues caused by the virus and spike protein. A biomarker of micro clotting, D dimer, was determined to be substantially elevated in many people who suffered from COVID-19 and particularly the spike protein injection. D dimer, fibrinogen degradation levels, and the prolonged prothrombin time were associated with poor prognosis in these patients and are caused by excess coagulation - all of which occur in the glycocalyx.¹⁶

Supplements are being formulated to improve the health of the glycocalyx. However, the best approach is to avoid its deterioration in the first place. This is where the constellation of the Japanese lifestyle comes into play. However, for those unable to live in that style, supplements support this structure.

One glycocalyx supplement is made with a brown seaweed called *Laminaria Japonica*. A certified extract is produced with a minimum extract rate of 85 percent of the compound fucoidan sulfate. Fucoidan sulfate is validated as a hybrid of heparan sulfate and chondroitin sulfate and has a high binding affinity with heparinase. Well-formulated supplements also contain high molecular weight hyaluronan, essential to provide the glycocalyx with its structural stability and dimension.

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Significantly, heparinase activity correlates with the metastatic potential of cancer cells, a concept that is now well-supported experimentally and clinically. Heparinase alters the glycocalyx surfaces of the blood vessels of the kidneys, thereby facilitating the development of albuminuria - a sign of kidney disease - and kidney inflammation. Heparinase-mediated glycocalyx degradation affects local organ dysfunction during critical illnesses such as sepsis. Still, the heparan sulfate fragments released during glycocalyx degradation may also impact multi-system organ injury and their ability to repair.

The fucoidan improves the glycocalyx breakdown with one mode of action inhibiting the heparinase activity. High glucosamine sulfate doses are essential for glycocalyx synthesis and reconstruction. Simply put, glycocalyx destruction is the underlying mechanism of many inflammatory diseases and explains why maintaining a healthy glycocalyx and repairing this structure is a crucial component of longevity.

Micronutrients and Health

Iodine and fucoidan are micronutrients. Deficiencies in micronutrients are under-appreciated as drivers of hunger. Hunger broadly represents a deficiency. An article by TrainingPeaks says it all.¹⁷ "Lay off the calorie-counting and focus on nutrients instead. You will likely enjoy more satiety, less inflammation, and better recovery. Density is a degree of consistency measured by the quantity of mass per unit of volume or the proportion of one substance concerning a whole. Therefore, nutrient density refers to the number of nutrients concerning the total quantity of a particular food, usually measured by the number of calories.

"Low-caloric food containing plenty of macro-and micronutrients is considered more "nutrient-dense" than high-calorie, nutritionally poor food, and many consider this a measure of overall food quality. Besides general health, nutrient density is also important for athletes hoping to optimize their fueling strategy."

"Where did you learn that?" As a scientist, I often ask people how they came about their beliefs. Our beliefs about health must be founded on root-cause, scientifically grounded principles. Your brain is your internal doctor. Most of us do not give our brains enough credit for the efforts it is making on behalf of our health. People in the developed world have moved away from nature in favor of convenience. In essence, we have lost touch, to some degree, with nature.

Consider how birds are more aware of a looming storm while humans rely on Channel 5. Further, we are bombarded with messages from companies selling their products. There is an adage, hear something enough times, and it becomes the truth – at least in the recipient's mind. This is referred to clinically as the "illusion of truth." A fundamental illusion of reality is that we are hungry because we lack calories. You do not have to look very far to determine that it is a false narrative, as two-thirds of U.S. adults are either overweight or obese.

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This concept of “illusion of truth” has everything to do with health and is all connected to your brilliant brain. What do you reach for when you feel hungry, and what are you thinking? I almost guarantee that you think you are lacking calories for energy. But is this the only, or even the principal, reason hunger occurs? How nutrients are stored in our bodies varies. Water-soluble nutrients, such as vitamin C and the B family of vitamins, are not stored well, so you need a steady supply of these. But fat-soluble nutrients, including; A, D, E, and K, are a different story. These are stored in the liver and fatty tissues of the body, so they do not need to be consumed every day. The liver stores vitamin D to supply an ample amount during the shorter days of winter, for example, when your skin cannot manufacture enough vitamin D.

Water-soluble vitamins are not appreciably stored in the body (except for vitamin B12) and thus must be consumed regularly in the diet. If taken in excess, they are readily excreted in the urine. Minerals constitute about 4 to 6 percent of body weight, with about one-half as calcium and one-quarter as phosphorus (phosphates), the remainder being made up of the other essential minerals that must be derived from the diet. Minerals not only impart hardness to bones and teeth but also function broadly in metabolism as electrolytes controlling the movement of water in and out of cells, as a driver of cellular electricity, balancing the pH of blood, as components of enzyme systems, and as constituents of many organic molecules.

Our farmlands have been overworked, and many nutrients and minerals have been lost or reduced to inadequate levels for optimal human health. Two very different books to read on this subject are *The Grapes of Wrath* and *Sea Energy Agriculture*. Where have those nutrients gone? They have followed the fundamental laws of nature, in this case, gravity, and have found their way into the oceans. While the land is depleted, the sea is rich in nutrients. This is an important reason behind the longevity of the Japanese.

Japanese Longevity

Japanese longevity is not just about the sea. Here are some other Japanese longevity quick facts. The list is quite extensive, and all of them play some role in longevity.

- Most of the population drinks green tea daily. It is served everywhere, and the most popular item in drink vending machines is green tea.
- Japanese eat smaller food portions than Westerners, and nutritional education focuses on balance. The narrative is not directed by a USDA equivalent that subsidizes junk food.
- They eat more sea flesh compared to land meats.
- Most eat fermented foods daily, especially fermented soy in miso soups.
- Japan is also a bath culture; soaking in baths relieves stress and improves circulation.

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- Natural Hot Springs are ubiquitous, and most have substantial minerals good for the skin.
- Everyone has access to affordable and top-notch health care.
- Adults pay 30 percent of their healthcare bill, thus incentivizing them to be healthy to reduce their costs.
- Kids learn personal responsibility and self-sufficiency at home and in school.
- Most children either walk or bicycle to school. The government has been operating radio routines for decades where citizens follow workouts through a live radio broadcast in schools, parks, and other open spaces.
- Respect for elders and other people is part of their culture and is taught at home and in schools. Japan has a holiday called "Respect for the Aged Day. And in Japan, senior citizens are "Living Treasures."
- Violence and gun-related deaths are almost non-existent in Japanese society.
- The government also respects elders and sends them silver "Sake Cups" when they reach 100 years old. Six of the top 10 and twelve of the top 20 oldest people alive live in Japan in 2020.
- In Japan, it is not uncommon for elders and retirees to toil physically until their final days.
- Japanese children are taught to eat a balanced diet through a mandatory educational program that does NOT emphasize low fat.
- There is a formal exercise education program to establish lasting behavioral patterns.
- It is currently nearly impossible to become a fast-food addict in Japan. The big U.S. chains have footprints in this country but do not dominate the market.
- In Japan, food is regarded as a gift from the land. To enjoy a meal is to pay tribute to the one who prepared it.
- They follow Hara Hachi Bu's rule, which is to stop eating when 80% full.
- Geographically, the islands of Japan are diverse, and their farming communities produce a wide variety of fruits, vegetables, and meats.
- Diversity applies to their choices of sea vegetables and sea flesh. How many people from the U.S. have consumed eel or sea urchins?
- The Japanese and other Asian cultures eat slowly. Try wolfing down a meal with chopsticks.

Ikigai is a Japanese concept of a reason for being. The focus is on four elements: 1) what you love, 2) what the world needs, 3) what you are good at 4) what you can be paid to do. Substantial research illustrates the relationship between life purpose and longevity.

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As a consequence of Ikigai, the Japanese describe craftsman as Shokunin, which means mastery of one's profession. All people, regardless of their tasks, are respected when practicing Shokunin.

There is LESS of a hierarchy in Japan and, consequently, MORE social cohesion. There are still social hierarchies, but it is more common in Japan for folks at different parts of the hierarchy to interact regularly and be friends with each other. In addition, people in different parts of the hierarchy tend to share the same values. They have much fewer social divides compared to the United States.

Shinto is the indigenous faith of the Japanese people, is the religion of nature, and is an optimistic faith, as humans are thought to be fundamentally good. Evil is believed to be caused by evil spirits. Shinto-Japanese people worship every small thing in nature; a rock, a river, and a tree branch all possess an inner spirit. Each part of nature has its individuality, but it is not separated from others and is all part of continuous collective life.

The Japanese view age more as a state of mind so that when they get older, they do not consider themselves as old they keep their bodies active and well-fed and their minds busy. Their elders are not choking in nursing homes.

The people of Japan are long-lived, and the reasons are numerous. An important point illuminated by the list above is that the government plays an active role in the longevity of its citizens. In contrast, the United States government policies support the profits of big businesses and are contrary to longevity.

So much for government for the people by the people!

Korea

Koreans are experiencing the most significant improvement in longevity. They have yet to pass the Japanese in longevity, but their trend indicates they may in the next couple of decades. An article titled "Future life expectancy in 35 industrialized countries: projections with a Bayesian model ensemble"¹⁸ explains the upward trend in Korean longevity.

"There is a 90 percent probability that life expectancy at birth among South Korean women in 2030 will be higher than 86.7 years, the same as the highest worldwide life expectancy in 2012, and a 57 percent probability that it will be higher than 90 years.

Projected female life expectancy in South Korea is followed by those in France, Spain, and Japan.

There is a greater than 95 percent probability that life expectancy at birth among men in South Korea, Australia, and Switzerland will surpass 80 years in 2030 and a greater than 27 percent probability that it will surpass 85 years.

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Of the countries studied, the USA, Japan, Sweden, Greece, Macedonia, and Serbia have some of the lowest projected life expectancy gains for both men and women."

Remember that Japan is at the top of the longevity list, where it is hardest to make significant gains. Whereas the United States is ranked 46th in longevity. Over the past several years, life expectancy in the United States has changed little and, in some years, declined. If you want to live a long healthy life, mimic the Japanese AND Koreans. The Koreans have similar sea-based diets to the Japanese, and they also consume a very wide variety of fermented foods.¹⁹

The unique geographical location of Korea and the isolation from neighboring countries imposed by rugged mountains from the North and the rocky ocean from the East, South, and West largely contributed to the development of a homogenous population and culture. Through time, simplicity has become a basic notion of Korean philosophy. This simplicity is also reflected in food habits. A fundamental aspect of this culture has been preserving fish, meat, pulses, and vegetables from times of abundance to times of scarcity through lactic acid fermentation.

Fermented Foods

For thousands of years, fermented foods have been a well-established part of the human diet, regardless of geography. Fermentation was much more prevalent in more northern regions due to the seasonal changes in food availability. Before electricity and the refrigerator and freezer, food was stored in just a few ways:

- Consuming large quantities during times of excess (feast and famine);
- Salting
- Cold storage underground, with or without ice, harvested from cold regions
- Fermentation (pickling).

Fermentation was initially done to increase the edible usage period of the food. It is uncertain when it was determined that fermented foods also contain more absorbable nutrients. We now know that fermented provides important nutrients that may not be obtained from the unfermented version of the food due to the limitations of the human digestion system. Digestion is a very rapid process, taking an average of 3.5 hours, whereas fermentation is a long, slow process. The two are similar but not necessarily comparable. However, consuming fermented foods and cooking is step 1 in the digestion process, followed by thorough chewing. These steps are essential to ensure the absorption of nutrient types that are hardest to absorb, namely micronutrients, including minerals. Fermented foods, in particular, have great potential to maintain health and prevent diseases. They also add desirable flavor and texture, reduction of toxicity, and decrease cooking time or eliminate the need for that step.

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Pickling was performed without much of an appreciation for, or an understanding of, the underlying microbial functionality and increase in nutrient bioavailability, until recently. The use of many organisms derived from these foods, and their applications in probiotics, have further illustrated their impact on gastrointestinal well-being and diseases affecting other sites in the body. However, despite the many benefits of fermented foods, their recommended consumption has yet to be widely translated to global inclusion in food guides. Thus, there is great variability in their type, quality, and consumption patterns on an international, national, and regional basis.

Most of us know the concept of picking or fermenting food, but what are they more precisely? Fermentation is a process of food preservation and alcohol production. Fermentation is primarily an anaerobic process converting sugars, such as glucose, to other compounds like alcohol while producing energy for the microorganism(s) or cells. Bacteria and yeast are microorganisms with the enzymatic capacity for fermentation, specifically, lactic acid fermentation with bacteria and ethanol fermentation with yeast.

Many different products worldwide result from fermentation, either occurring naturally or through the addition of starter culture. Various bacterial and yeast species are present in each case, contributing to fermented foods' unique flavors and textures. This is an important point in an overly clean world where the hygiene hypothesis explains that many modern diseases are initiated by humans being too clean. Also, unnecessary and overuse of important antibiotics and harmful chemicals consumed disrupt the gut microbiome.

Fermentation requires different bacteria and yeast, which implies that the diversity of organisms is important in fermentation and, by extension, the microbiome is critical. For example, consuming fermented dairy may help the situation if you are intolerant to dairy. However, whenever something new is introduced to a system that is in balance, optimal or not, there may be a reaction and disruption to that balance. Therefore, adding something like fermented dairy products may need to be done very slowly, starting with a low amount and working up as the gut environment acclimates to this new constituent.

We are all genetically 99.9 percent the same. Everyone should be able to tolerate dairy from this perspective. If someone cannot tolerate dairy, it is most likely because of inefficient digestion of that composition. The best way to solve this is to introduce organisms that naturally decay into the dairy - that being the organisms found in fermented dairy products.

Table 1 is a listing of the more common fermented foods and the countries from where these foods are thought to originate. The bacteria and yeasts in Table 2.1 are referred to as “probiotics” when they adhere to the following World Health Organization (WHO) definition:

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“Live microorganisms which, when administered in adequate amounts, confer a health benefit on the host.”²⁰

Examples of fermented foods and countries in which they are believed to originate and remain particularly popular.

Fermented Food and Main Constituents	Country
Yogurt—milk, <i>L. bulgaricus</i> , <i>S. thermophilus</i>	Greece, Turkey
Kefir—milk, kefir grains, <i>Saccharomyces cerevisiae</i> and <i>L. plantarum</i>	Russia
Sauerkraut—green cabbage, <i>L. plantarum</i>	Germany
Kimchi—cabbage, <i>Leuconostoc mesenteroides</i>	South Korea
Cortido—cabbage, onions, carrots	El Salvador
Sourdough—flour, water, <i>L. reuteri</i> , <i>Saccharomyces cerevisiae</i>	Egypt
Kvass—beverage from black or rye bread, <i>Lactobacillus</i>	Russia
Kombucha—black, green, white, pekoe, oolong, or darjeeling tea, water, sugar, <i>Gluconacetobacter</i> and <i>Zygosaccharomyces</i>	Russia and China
Pulque—beverage from agave plant sap, <i>Zymomonas mobilis</i>	Mexico
Kaffir beer—beverage from kaffir maize, <i>Lactobacillus</i> sp.	South Africa
Ogi—cereal, <i>Lactobacillus</i> sp., <i>Saccharomyces</i> sp., <i>Candida</i> sp.	Africa
Igunaq—fermented walrus	Canada
Miso—soybeans, <i>Aspergillus oryzae</i> , <i>Zygosaccharomyces</i> , <i>Pediococcus</i> sp.	Japan
Tepa—Stinkhead fermented fish	USA
Dosa—fermented rice batter and lentils, <i>L. plantarum</i>	India
Cheddar and stilton cheeses— <i>Penicillium roqueforti</i> , <i>Yarrowia lipolytica</i> , <i>Debaryomyces hansenii</i> , <i>Trichosporon ovoides</i>	United Kingdom
Surströmming—fermented herring, brine, <i>Haloanaerobium praevalens</i> , <i>Haloanaerobium alcaliphilum</i>	Sweden

Table 2.1. Examples of fermented foods and countries in which they are believed to originate and remain particularly popular.

The additional health benefits of fermented dairy products conferring compared to non-fermented dairy are multi-fold. The breakdown of proteins (proteolysis) that occurs in fermenting milk results in a higher content of peptides and free amino acids, especially cystine, histidine, and asparagine, which play various roles in health and produce a more digestible food than milk per se. The breakdown of lactose concentration by the bacteria containing β -galactosidase, not only in the fermentation process but also in the stomach when the bacteria die and release this enzyme, allows many lactose-intolerant individuals to consume the milk product.

Several fermented foods available in Korean cuisine have been studied to some extent. Among them, kimchi, chongkukjang, doenjang, ganjang, and gochujang may be regarded as characteristic ones. Moreover, kimchi has met worldwide recognition and commercial significance.

In general, lactic acid bacteria (LAB) from several genera, including *Lactobacillus*, *Streptococcus*, and *Leuconostoc* are predominant in fermented foods. Still, other bacteria, as well as yeast and fungi, also contribute to food fermentations. Commercially produced fermented foods frequently serve as carriers for probiotic bacteria, but not always. There still needs to be more clarity about which fermented foods contain live microorganisms. In many cases, an

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understanding of the role of these microbes on the gut microbiome is also only partially understood.

Fermented foods are made with the help of bacteria and are associated with healthfulness; thus, they are the same as probiotics, right? Probiotics are defined as live bacteria that confer health benefits when consumed in adequate numbers.

A particular food or beverage produced by fermentation does not necessarily indicate that it contains live microorganisms. Bread, beer, wine, and distilled alcoholic beverages require yeasts for fermentation. Still, the production organisms are either inactivated by heat (in the case of bread and some beers) or are physically removed by filtration or other means (in the case of wine and beer). Moreover, many fermented foods are heat-treated after fermentation to enhance food safety or to extend shelf-life. Thus, fermented sausages are often cooked after fermentation, and soy sauce, sauerkraut, and other fermented vegetables are made shelf-stable by thermal processing. Sourdough bread, canned sauerkraut, other fermented vegetables, and many chutneys are heat-treated, which inactivates the microorganisms. So, while these foods and drinks might still be flavorful and nutritious, they do not have probiotic activity.

Some products, like many commercial pickles and olives, are not fermented but placed into brines containing salt and organic acids, making the foods more easily digested. Even non-thermally processed, fermented foods may contain low levels of live or viable organisms simply due to inhospitable environmental conditions that reduce microbial populations over time. However, it is important to note that the absence of live microbes in the final product does not preclude a positive health benefit compared to the non-fermented counterpart. For example, food fermentation microbes may produce vitamins or other bioactive molecules. In addition, they inactivate toxins or other substances and reduce the toxicity of the food. The non-fermented versions of these foods, in these common cases, do not necessarily confer these benefits.

Not having live cultures does not imply that fermented foods are no better than their non-fermented versions. Indeed, live cultures have the potential to enhance the gut microbiome by contributing colony-forming units (CFUs) contained in the food. However, even if the fermented food was pasteurized, before that occurred, the organisms were "digesting" the food product and creating basic building blocks that ^{may} not be produced in an individual with an inefficient, or even an efficient, digestive system.

All this being said, many fermented foods contain live probiotic organisms. Dairy products like kefir and yogurt deliver beneficial bacteria to our gastrointestinal tracts, like most cheeses, non-heated kimchi, and sauerkraut. Kombucha and miso contain large numbers of viable bacteria that can provide a probiotic boost.

Not all vitamins and minerals are destroyed during thermal processing. Examples of thermostable vitamins are niacin and pantothenic acid. Foliates are more

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susceptible to heat, and LAB organisms can manufacture them. Many functional doctors recommend methyl folate and the methylated form of B12 if levels of homocysteine - a vascular toxin - are elevated. I have found that people with elevated homocysteine who take a variety of probiotics see a normalization of their level. This implies that many people suffering from elevated homocysteine levels are deficient in the suitable composition of B vitamins due to thermal processing or are inefficient at absorbing these nutrients. In either case, a diverse microbiome provides a solution.

Some studies suggest that a cup of yogurt once in a while or a spoonful of kimchi will not have much of a sustained impact on gut health. This variable depends on the health of the person consuming these foods and their level and causes of gut dysbiosis. In theory, a colony-forming unit is a colony-forming unit regardless of whether it comes from a manufactured probiotic or fermented food. Studies suggest that probiotic bacteria must be eaten regularly to maintain a presence among the microbes that have already staked their claim to valuable real estate in the gut. But, over time, the microbiome may establish a new normal based on the consumption of organisms. We will know for sure as more scientific studies are conducted.

Beneficial organisms may be your best defense against the pathogenic kind. There is evidence that fermented dairy products may have therapeutic properties in some people with severe *Clostridium difficile* infection by repopulating the gut with healthy bacteria and reducing the risk of the regrowth of harmful microbes. *Saccharomyces boulardii*, a yeast, is one such probiotic organism documented to reduce *C. diff.* concentrations.²¹

The Journal of the American Medical Association (JAMA) generally promotes and protects physician members and their use of pharmaceutical interventions. Oncology is particularly controlled due to the profits afforded to doctors by the treatments. According to an article by NBC News²² "It is a unique situation in medicine: Unlike other kinds of doctors, cancer doctors are allowed to profit from the sale of chemotherapy drugs. "The significant amount of our revenue comes from the profit, if you will, that we make from selling the drugs," says Dr. Peter Eisenberg, a private physician specializing in cancer treatment. Doctors in other specialties simply write prescriptions. But oncologists make most of their income by buying drugs wholesale and selling them to patients at marked-up prices. "So, the pressure is frankly to make money by selling medications," says Eisenberg."

"Brand-name chemotherapy is often incredibly expensive, in excess of \$100,000 per patient. Sometimes there are excellent generic alternatives, but many oncologists are hesitant to prescribe generics because such prescriptions cost them money. For many medicines, you see, oncologists receive a 6 percent markup, meaning when they infuse a patient with a \$10,000 monthly course of chemotherapy, their practice yields an extra

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\$600. By contrast, if the practice treated that patient with generic chemotherapy, they'd be out most of that extra money."²³

In an unexpected departure, JAMA Oncology published a paper that potentially provides a path away from traditional treatments within traditional oncology. The article's title is "The Potential of the Gut Microbiome to Reshape the Cancer Therapy Paradigm."

Here is the abstract:

"Importance: The gut microbiome, home to the vast kingdom of diverse commensal bacteria and other microorganisms residing within the gut was once thought only to have roles primarily centered on digestive functions. However, recent advances in sequencing technology have elucidated the intricate roles of the gut microbiome in cancer development and the efficacy of therapeutic response that need to be comprehensively addressed from a clinically translational angle.

Observations: This review aims to highlight the current understanding of the association of the gut microbiome with the therapeutic response to immunotherapy, chemotherapy, radiotherapy, cancer surgery, and more while contextualizing possible synergistic strategies with the microbiome for tackling some of the most challenging tumors. It also provides insights into contemporary methods that target the microbiota and the current progression of findings being translated from bench to bedside.

Conclusions and Relevance: Ultimately, the importance of gut bacteria in cancer therapy cannot be overstated in its potential for ushering in a new era of cancer treatments. With the understanding that the microbiome may play critical roles in the tumor microenvironment, holistic approaches that integrate microbiome-modulating treatments with biological, immune, cell-based, and surgical cancer therapies should be explored."

Nature magazine also delves into the microbiome as a potential cancer therapy - at any point along the cancer continuum. In the article titled, "How gut reactions are shaping cancer treatment,"²⁴ the authors explain the following. "Cancer treatment is no longer the domain just of oncologists. It now also involves microbiology, artificial intelligence, diet and nutrition, genomics, bioinformatics, and computing specialists. Work at Sloan Kettering and Stanford is revealing how the gut microbiome can make the difference between treatment success or failure."

Beyond cancer, other health benefits of fermented foods have been intensively investigated. Identifying bioactive peptides and microbial metabolites in fermented foods that can positively affect human health have consolidated this interest. Each fermented food typically hosts a distinct population of microorganisms. This concept of a "distinct population" is the key. Consuming a variety of fermented foods provides wide diversity to the microbiome community.

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Once ingested, nutrients and microorganisms from fermented foods may survive to interact with the gut microbiome, which can now be resolved at the species and strain level by metagenomics. Transient or long-term colonization of the gut by fermented food strains or impacts of fermented foods on indigenous gut microbes can be determined.²⁵ The abstract and key sections from the article "Fermented Foods, Health and the Gut Microbiome" are provided here.

"Fermented foods have been a component of the human diet from ancient times. Among the earliest evidence for the deliberate application of fermentation has been found in pottery vessels discovered in China dating from 7000 BC that were used to ferment rice, honey, and fruit. However, it is likely that inadvertent production and consumption of fermented foods significantly predate this, as foods must have undergone spontaneous fermentation during storage.

While microorganisms, first discovered in the 1670s by Antoni van Leeuwenhoek, originally received much attention as agents of food spoilage and disease, practical applications, including their ability to produce antibiotics against pathogenic bacteria and to impact human health positively, were soon discovered. However, the most important function that microbes have played throughout human history is their involvement in food preservation via fermentation.

Fermentation is the process whereby alcohols, carbon dioxide, and organic acids are produced by microorganisms, primarily from sugars and under mostly anaerobic conditions, for energy production. The accumulation of alcohol and organic acids and the associated increase in acidity of the food substrates inhibits the growth of other microorganisms and the activity of enzymes in the food system, thus reducing the rate of spoilage and resulting in foods with extended shelf-life.

Fermented foods have become associated with health benefits as well. One of the earliest proponents of this hypothesis was Élie Metchnikoff, who was interested in the potential of food to promote the elongation of life. In Metchnikoff's essay entitled 'Lactic Acid and Putrefaction,' he attributes the long lives of Bulgarian peasants to the staple foods of the country at the time, particularly soured milk. His experiments elucidated that lactic acid bacteria (LAB) cultures in the fermented food produced 'disinfecting bodies' beneficial to their human host. Thus, fermented foods have been linked positively with human health.

Beginning in the early 1900s, the mechanisms subsequently postulated by which these foods can benefit health include one or a combination of the following: (i) the direct nutritional value of fermented foods, including bioactive compounds, produced as a consequence of the fermentation process; (ii) provision of nutrients to promote the growth of indigenous gut microbes; and (iii) the capacity of the microbes in fermented foods to survive gastric transit and to either become a component of the gut microbiome or to inhibit/compete with existing members of the gut microbiome.

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It is difficult to establish the number of fermented foods produced globally definitively. Most estimates suggest that there are more than 5000 different kinds. However, this figure will likely expand significantly when local and regional variations are considered. For example, different classification schemes can be used to classify cheese. While certain approaches suggest as few as eighteen primary cheese types when local modifications based on variations in procedures, microorganisms, and milk types are considered, it is generally accepted that more than 1000 cheese varieties are available globally.

Different approaches have been used to characterize or group fermented foods, the most common of which are based on the raw/non-fermented food substrate, resulting in groupings of fermented foods made from cereals, vegetables, legumes, roots/tubers, milk, meat, fish, alcoholic beverages, and miscellaneous raw materials."

Interestingly, some commercially fermented products have organisms that were not intentionally added to the formulation. These are referred to as non-starter microbiota and are indigenous bacteria or a contaminant of manufacturing. High-throughput DNA sequencing technologies reveal highly diverse populations of both starter and non-starter organisms. This information also indicates that natural organisms we often view as harmful are more often beneficial.

Here is a personal example. I established a garden in the clay soil of East Tennessee. I added a substantial amount of horse manure to the soil one fall. In the summer, I harvested various root crops, including carrots. Instead of copiously washing some of the yields, I incompletely wiped off the dirt adhering to the carrots and ate them. I experienced no adverse symptoms of toxicity, and I do not take probiotics. I do consume a wide variety of fermented foods. Decomposing horse manure was visible in the soil. I know you are saying, "How disgusting!". But I believe that most things in nature are beneficial, and most things presumed to be harmful were put there by humans and thus must be classified, in many cases, as unnatural.

An article titled "Fermented Foods as a Dietary Source of Live Organisms" is the most comprehensive survey of the published literature on these foods and the types of organisms found in them. More than 140 studies were included in the analysis. Although the literature from which the results were assembled covers 50 years and a range of different regions and methodologies, the results are stated to be "remarkably consistent."

Yogurt

"Studies were conducted for retail or commercially manufactured yogurts and other cultured dairy products obtained in the U.S., Australia, Spain, France, Norway, Greece, Argentina, and South Africa. All the yogurts examined contained the yogurt culture organisms *S. thermophilus* and *L. delbrueckii* subsp. *bulgaricus*, at levels ranging from < 10⁴ to 10⁹ CFU/g or ml. In general, counts

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for *S. thermophilus* were somewhat higher than for *L. delbrueckii* subsp. *bulgaricus*. In several studies, other microorganisms, including *Bifidobacterium* spp. and *Lactobacillus* spp., were also enumerated. Levels of the latter ranged from undetectable (< 10 CFU/g) to 108 CFU/g. The addition of these probiotic bacteria did not appear to have any effect on the levels of the yogurt culture organisms. Although most studies reported counts at only a single time point, other studies reported initial counts and second-time points, usually considered end-of-shelf-life. In such cases, counts were generally similar at both time points (>10⁶ CFU/g), provided samples were stored at refrigeration temperatures."

"The number and type of live microorganisms in other cultured dairy products have also been reported. These include kefir, cultured buttermilk, and simply "fermented milk." As for other cultured dairy products, LAB populations were in the 10⁵–10⁹ CFU/g range."

Cheese

"Levels of lactic acid and related bacteria were reported for more than 30 types of cheese from 18 countries, including the United States, Italy, France, Germany, Mexico, Ireland, and South Africa. Microbial counts ranged from undetectable (< 10³ CFU/g) to 10⁹ CFU/g, with the highest levels found in Tilsit cheese (typically aged 2–4 months). In contrast, Grana Padano aged one year, Parmesan aged greater than one year, and Swiss Gruyere aged greater than one year all showed no detectable microorganisms (< 10³ CFU/g)."

Fermented Meats

"Most samples were from the United States, Spain, Portugal, and Italy and were composed of pork and beef. The levels of microorganisms (LAB and total) ranged from undetectable (< 10² CFU/g) to 10¹⁰ CFU/g. Data were reported as either within the product shelf life or after the ripening or maturation of the sausage. Counts of viable microorganisms in sausages from the United States were generally lower (< 10⁷ CFU/g) than in sausages from other countries. In particular, LAB levels were all < 10⁶ CFU/g".

Fermented Vegetables

"Fermented vegetables included sauerkraut, olives, mustard pickles, pickles, and kimchi. Laboratory-manufactured products using industrial or traditional practices were included due to the need for more literature on fermented vegetables from retail sources. Microbial counts for sauerkraut were generally reported as LAB, ranging from 10³ to 10⁸ CFU/g."

"Other products for which quantitative data were reported included mustard pickles and kimchi from Taiwan and pickled cucumbers from China, India, and the United States. Microbial counts ranged from undetectable (< 10¹) to 10⁸ CFU/g."

Fermented Tea (Kombucha)

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"Kombucha is a fermented beverage made from sweetened tea to which a specialized culture is added. The latter comprises a symbiotic culture of bacteria and yeast or SCOBY, normally within a cellulose-type membrane. Bacteria commonly found in kombucha include the acetic acid bacteria belonging to the genera, Acetobacter, Gluconacetobacter, Gluconobacter, and LAB. Most of the yeasts associated with kombucha are species of Saccharomyces, although other yeast genera may also be present. This product is now widely consumed, and manufacturers promote the presence of live microorganisms on product labels. However, there are few published data on the levels of microbes present in retail products. In general, acetic acid bacteria levels ranged from 10^6 to 10^7 CFU/mL at the end of the fermentation, and similar counts were reported for LAB and total aerobic bacteria. Total yeast counts of about 10^7 CFU/mL were also reported."

"The human gastrointestinal tract is home to more than 1012 microbes and up to 1000 different species types. This diverse ecosystem provides protection against pathogens, extracts nutrients from dietary components, and modulates the immune system. The gut microbiota is also very stable, although several factors, including exposure to antibiotics, stress, and disease, can disrupt this community, leading to dysbiosis. The ability of diet and dietary components to modulate the gastrointestinal microbiota, redress dysbiosis, and enhance human health is now well-established."

What is the right number specified in a healthy gut microbiome? That question is without a definitive answer, but the more, the better. A well-known function American health author and entrepreneur produced a video on the microbiome and indicated that testing showed 160 unique species in his gut. He noted that his gut was optimal. However, this is an inadequate level of diversity. Time will tell, as this type of testing is not necessarily comprehensive and accurate. The number of organisms he has may be much higher as testing improves.

Fecal Transplants

Fecal Microbiota Transplantation is the infusion of fecal matter from healthy people to rehabilitate an insufficient microbiome. A fecal transplant is the infusion of a super probiotic.

Thomas Borody, M.D., is a pioneer in FMT and is most famous for his groundbreaking work developing the triple therapy cure for peptic ulcers in 1987, which has saved hundreds of thousands of lives. Doctor Borody founded the Centre for Digestive Diseases (CDD) in 1984 after a distinguished career with leading hospitals, including St Vincent's in Sydney and the Mayo Clinic in the USA. He is a world-renowned leader in the clinical microbiota field dating back to 1988, when he started performing what is now called Fecal Microbiota Transplantation.

FMT research has shed light on the population and the optimal healthy microbiota of the gut. A study titled "A human gut microbial gene catalog established by

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metagenomic sequencing” is one of just a few that evaluates the breadth of the microbiome. A summary of the key findings is included here:

- One hundred and twenty-four healthy Europeans were fecal donors for the study.
- Collectively 1,000 and 1,150 prevalent bacterial species were identified.
- Each individual has at least 160 bacterial species, which are also primarily shared.

Importantly, note that the catalog was bacterial only, so fungal and yeast organisms are not included in this study's makeup of the microbiome. However, based on these data, our entrepreneur's microbiome may be optimal.

Another study used sophisticated species-level analysis. Similar to the study cited above, a total of 1,235 species were classified in the feces of 120 healthy Chinese individuals, including 461 previously classified species, 358 potentially new species, and 416 potentially new taxa, which were categorized into low, medium, and high prevalent bacteria groups based on their prevalence. Each individual harbored 186 unique species, on average. There was no universal bacterial set of species shared by all the individuals. However, a significant number of organisms were common in most people. Again, only bacterial organisms were included in this study.

Open Biome is an American non-profit dedicated to expanding safe access to fecal microbiota transplantation (FMT) and catalyzing research into the human microbiome. The initial efforts of this organization are to make FMT available to half a million Americans infected with *C. difficile* each year. About 1 in 5 do not respond to antibiotics, but (FMT) is a promising new therapy, curing over 85 percent of cases with recurring *C. difficile* - making it *C. not so "difficile"* to eradicate.

Dr. Julian Kenyon, founder of the Dove Clinic in Winchester, UK, administered FMT until COVID-19 halted this therapy. In the United States, organizations like the Mayo Clinic use FMT, as do other organizations found on the openbiome.org website. Still, their use is restricted to those with potentially life-threatening conditions. Dr. Kenyon's FMT protocol was as follows:

Standard treatment protocol for FMT

"We administer two to three times per week, although if the patient is coming from a long distance or from abroad, then we do it daily for five days one week and five days during the next week. It is not essential that the days have to be consecutive, and this program can be modified, but generally speaking, the first ten doses need to be given reasonably close to each other. Two treatments a day is not recommended because even though this may shorten the treatment process, this does not allow the gut time to accommodate the new microbiome." This last statement is important and applies equally well to oral probiotics.

Probiotics

In general, the approach to populating or expanding the microbiome with probiotics, including fermented food and commercially produced probiotics, is performed in this manner.

- Evaluate the gut for dysbiosis. This can include any combination of symptoms, blood labs, and stool samples.
- Even the mildest symptoms should be considered and documented. On the continuum of diarrhea, if a person is eliminating more than once a day, they may have mild gut dysbiosis.
- Blood labs include H-pylori, markers of intestinal permeability, and the ESR test.

Start introducing broad strains of organisms. The dose depends upon the level of gut dysbiosis determined in the evaluation phase. The more out of balance, the more slowly the organisms must be introduced. Slowly, in this context, means both time and concentration.

Probiotic administration.

Strategy ONE: Introduce small amounts of various probiotic substances, including commercial probiotics and fermented foods. However, on each day of a 7-day schedule, only one probiotic substance is introduced. Strategy one continues until symptoms and labs show optimization. This program may be repeated periodically for microbiota maintenance.

Strategy TWO: This is for severe gut dysbiosis. Compared to Strategy ONE, even lower doses are used. For example, divide a capsule or cut a pill in half. And only one probiotic substance is introduced for the first week. A second probiotic may be introduced in the second week without introducing other substances, including the probiotic from the first week. This process of weekly inoculations of one probiotic is continued for a minimum of seven weeks. Then the entire process is reinitiated at week 8 with the probiotics used during the first week. When positive results are realized, the person may switch to Strategy ONE.

- Retest periodically and consider doing Strategy 1 prophylactically, annually, for a month or more.

Some current research asserts that organisms delivered by fermented foods are transient (short-lived). In microbiota research, the definition of normal microbiota is organisms that are always present in or in the body and are usually harmful ones. Based on this definition, organisms from fermented foods are not technically transient. However, the research on fermented foods indicates they are not normally long-lived in the gut and require constant or frequent consumption. In this sense, organisms delivered through fermented foods are not considered colony-forming. However, this area of study is in its infancy, and these conclusions may be proven to be incorrect in the future.

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The good news is that even those who assert fermented food organisms as transient also agree that they improve health. The following statement explains this. "If present, fermentation-derived microorganisms, despite their transient nature, may have the potential to influence gut microbiota diversity, structure, and function.²⁶ Notably, they may also affect health due to their ability to out-compete pathogens for resources, produce short-chain fatty acids from available carbohydrates, secrete anti-microbial agents, contribute to immune homeostasis, and produce vitamins."

A key paper attempting to address fermented foods and the gut microbiota states,²⁷ "The results presented in this systematic review suggest that a complex interplay between food and gut microbiota is indeed occurring, although the possible mechanisms for this interaction, as well as how it can impact human health, remain a puzzling picture.²⁸ It is an interesting dilemma and begs the question, whence come the most beneficial organisms? There can be only so many sources, as these organisms did not spontaneously appear. Here is a short list, and there may be many more.

- From mom (and dad) - but where did they come from?
- From the environment - while in utero and once born and exposed to the environment. Airborne particles may contribute to the population and re-population of the gut. Daily, humans swallow up to 1.5 liters of saliva each day. Airborne organisms adhere to the saliva and are then swallowed.
- From food - any raw and even lightly cooked food contain organisms. Are the organisms in raw or cooked food the same as those in the fermented version? Is this known?

Except for the one-time exposure to mom's microbiota, the other sources are ongoing and provide a way to sustain the microbiome. It seems logical, then, that being in nature often, exploring different environments, and consuming a variety of foods, has the potential to expand your microbiota. Variety is the spice of life.

There is no question that fermented and probiotic consumption is associated with improvements in health status or reductions in disease risk. Examples of health conditions and symptoms improvement from the medical literature include:

- metabolic syndrome;²⁹
- bladder cancer;³⁰
- reduced weight gain;³¹
- reduced incidence of asthma and atopic dermatitis;³²
- reduced risks of type 2 diabetes and high blood pressure among Japanese adults.

Do objective physiological markers of health improve on probiotic regimens alone? Several reports provide evidence that fermented foods, such as kimchi, fermented soy products, and yogurt, can improve important biomarkers of health.

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- Fasting blood glucose and other metabolic syndrome symptoms in overweight and obese adults consuming Kimchi³³
- Fasting blood glucose improvements were observed in healthy adults³⁴
- Plasma triglyceride levels in obese adults³⁵
- Improved lactose tolerance due to in vivo expression and release of β -galactosidase by the yogurt culture microbes³⁶

Objective data on probiotic effects on physiology are still in the purview of medical research on animal models. These are woefully inadequate to predict human health in this area. This is a guess, but when I observed what my dog could eat without ill effects, I knew she was not a good model for me. As I am sure you know, dogs can eat rotten things that make humans very sick. However, I have thought about a fecal transplant from animals to humans. This will be done in the future. Any volunteers?

Our data on biomarker improvements using the probiotic program described above, which is not a clinical trial, but rather real-world experience, unequivocally and consistently shows improvements in the following biomarkers:

- Erythrocyte Sedimentation Rate;
- C-reactive protein;
- Homocysteine;
- Free iron and ferritin;
- Other micronutrients.

This list will continue to expand because breaking down and absorbing nutrients is key to all aspects of health. Do not just rely on randomized clinical trials for results on the physiological benefits of probiotics and the expansion of your microbiota. There is little, if any, funding for this type of research. Instead, rely on common sense and mechanisms of disease. Repair and recovery are the most fundamental process that keeps us healthy for up to 120 years. Pro- and prebiotic foods contribute significantly to these mechanisms.

There is a myriad of reasons for the longevity of Japanese and Korean citizens. The usual suspects play major roles - diet and exercise. Having a purpose is another key element. Sadly, government and culture are working against longevity in the West, whereas it works in favor of longevity in the East. Longevity data illustrate this quite clearly.

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"The best and most efficient pharmacy is within your own system.

- Robert C. Peale

What is Immunity

Understanding the fundamentals of immunity: innate, adaptive, and barrier immunity is important because immune responses are an indication of what type of assault (insult) is underway in our body. If tests are not determining the degree of immune response and treatments are not based on improving immunity status, then the process is symptomatic, not a root cause, and the patients will not achieve the outcomes they desire.

Our immune system serves a very important purpose, to keep us alive. In doing so, it prevents disease. Chapter 2 highlighted the strong connection between longevity and morbidity. The immune system, like any other part of our body, is made up of cells and molecules. The components supporting our cells, the building molecules, must either be obtained from food (essential nutrients) or synthesized in our body from essential nutrients, in our liver, for example. The strength of the immune system is dependent upon these nutrients. A healthy immune system and a healthy you are intimately tied to maintaining homeostasis which is only achieved if there are no building block (nutrient) deficiencies. When that is not the case, our bodies can slip into a state of “dis ease.”

At the beginning of the COVID outbreak, the global narrative was on immune health. Each of us have control over our immune health, thus on the severity of the disease experienced. Then the narrative suddenly switched to vaccines, almost as if a playbook was being orchestrated and followed. Vaccines are part of an immune system augmentation approach, specifically on that of the adaptive immune component. The work Dr. Brian Hooker and Neil Miller have performed is a true evidence-based review of vaccines. Their work is important to read and understand regardless of your stance on vaccines.

Before COVID-19, the definition of a vaccine adequately described their intent, to enhance adaptive immunity against a specific pathogen.

The definition of a vaccine and a vaccination in 2020 was,

Vaccine: "Inoculants that produce immunity to a specific disease."

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Vaccination: "The act of introducing a vaccine into the body to produce immunity to a specific disease."

The new definition now reads,

Vaccine: "A preparation that is used to stimulate the body's immune response against diseases."

Vaccination: "The act of introducing a vaccine into the body to produce protection to a specific disease."

This change to a single word in the vaccination definition has major ramifications. The intent by those responsible for the change was to provide forgiveness when the COVID-19 vaccine inevitably did not provide any significant or lasting immunity. However, any substances, natural or synthetic that improves health, thereby protection across a range of diseases including a specific disease, technically meets the definition of a vaccination. Another translation of new definition is, if you improve your immune system, you are vaccinated. If you take vitamin D, you have most likely met the definition of being vaccinated.

Every synthetic substance, when introduced into your body, has side effects. Pharmaceutical drugs cause a shocking high number of side effects. The drug industry reports "adverse events" on the fine print of packing inserts. The average number of adverse events listed on a drug's package insert is 69. Sixty-nine! If that was the true number, never take a drug again. However, that is NOT the right number. Researchers at Stanford Medical School created publicly available databases of their work, one of which is called "OFFSIDES." The OFFSIDES database documents an average of 329 new adverse events for each of the 1,332 drugs included in the system. The Stanford number of 329 compared to the manufacturer's number of 69 reflects a 500% underreporting of adverse events or side effects.

Pfizer, in their report titled, "5.3.6 CUMULATIVE ANALYSIS OF POST-AUTHORIZATION ADVERSE EVENT

REPORTS OF PF-07302048 (BNT162B2) RECEIVED THROUGH 28-FEB-2021" report 1290 "adverse events of special interest."³⁷ This only reflects data from the first several months of the vaccination program. And the Pfizer COVID-19 shot is not the only one being used. Collectively, the Pfizer product accounts for approximately 60% of those administered.³⁸ The value, 1290 represents a 2000% increase compared to drug adverse events reported on packaging inserts. Yet, these vaccines are exempt from any liability per Congressional rule while drugs are subject to liability claims.

Good nutrition, natural supplements, and exercise improve immunity, meet the definition of a vaccine and vaccination, and have no side effects. Further, with good health, the likelihood of dying in a pandemic dramatically drops - by at least 1000% in COVID-19. And, being exposed to the virus provides lasting immunity

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across a wide range of potential variants. In this context, being exposed to the SARS-CoV-2 constitutes vaccination. Improving immunity and being exposed to a virus is vaccination at its finest.

The FDA says, "The United States' long-standing vaccine safety system ensures that vaccines are as safe as

possible.³⁹ Note, this statement does not mean they are safe. According to the CDC when a vaccine goes through standard health and safety protocols, they are often safe. Note "often" does NOT mean always. However, the narrative about immune health was completely dropped. We know why. To get emergency use authorization, there must be a pandemic.

Why was COVID-19 able to be classified as a pandemic?

The U.S. population is unhealthy, thus vulnerable to the virus. Chapter 1 and subsequent chapters explains that our existing healthcare system is actually designed to make us and keep us chronically ill.

What triggered emergency use authorization to speed the development and allowance of vaccines without the usual time to conduct adequate safety studies?

Available off-label drugs and early treatment was discouraged leading to high hospitalization and death rates.

These two situations are important examples of health freedom lost.

Infection and Immunity

The main, and arguably, only purpose of our immune system is to protect us from infection. Here are some statements on our immune system from various respected sources.

Cleveland Clinic: A well-working immune system prevents germs from entering your body and kills them or limits their harm if they get in. To keep your immune system healthy, get plenty of sleep, stay active, eat healthy foods, keep your weight under control, reduce your stress and follow other healthful habits.⁴⁰

WebMD: This network of tissues, cells, and organs first tries to keep out germs like bacteria, viruses, fungi, and parasites and then deals with them if they manage to get in. If it senses something in your body that could be bad for you, it triggers the release of special cells. These travel to where the trouble is, attack the intruder, and help get rid of it⁴¹.

Pfizer: The immune system's job: defend against disease-causing microorganisms. Its goal is to keep us healthy. The immune system is a vast and complex interconnected network of many different organs, cells and proteins that work together to protect the body from illness. A healthy immune system can defeat invading disease-causing germs (or pathogens), such as bacteria, viruses, parasites—as well as cancer cells—while protecting healthy tissue.

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Understanding how the immune system works and how we can help protect our bodies is essential to the fight against the COVID-19 pandemic.⁴²

Comment: Hmmm – Why are the preponderance of drugs Pfizer produces NOT treating infection or supporting the immune system? And, why isn't this message from Pfizer in the headlines instead of the vaccine? According to National Public Radio (NPR),

"COVID vaccines are set to be among the most lucrative pharmaceutical products ever."⁴³

CDC: It's almost impossible to find a basic definition of immunity from them. All the top hits within the CDC website are focused on driving the discussion to vaccines. However, this definition did appear within the Agency for Toxic Substances and Disease Registry: "The immune system consists of white blood cells, the thymus, the spleen, lymph nodes, and lymph channels. It provides immunity to the body from bacteria, viruses, parasites, and tumors by producing B lymphocyte and T lymphocyte cells)."⁴⁴

National Institutes of Health: The overall function of the immune system is to prevent or limit infection.⁴⁵

Mayo Clinic: The immune system is designed to execute rapid, specific, and protective responses against foreign pathogens.⁴⁶ The Mayo Clinic supports the notion that deficiencies impact immunity. A good diet is "important to maintain a functional immune system by avoiding immunodeficiency due to malnutrition or micronutrient deficiencies."

Summary: Immunity fights infection and is compromised by deficiencies. Most of us do not have a vaccine deficiency, but we do have nutrient deficiencies.

Very often, authoritative sources, like the ones sited above, will indicate that our immune system fights Cancer and autoimmune diseases. However, this is contradictory to their own statements about the action the immune system. The inference is our immune system is fighting these human named disease syndromes while not fighting infection.

Dr. Paul Ewald, an evolutionary biologist has written extensively on chronic disease causation. His thesis is elegant in its simplicity. A compromised immune system leads to stealth chronic infections and chronic diseases. He, of course, recognizes that very virulent infections cause acute symptoms and disease. But, his key point is that less virulent infections cause subtle diseases that slowly develop - that is, chronic diseases. In his book, *Plague Time*, he sets the tone for his brilliant treatise on what some call "the new germ theory."⁴⁷ In the introduction to the book titled, "The Culprits," He writes:

"Surely the horror of deadly plagues able to carry away incomprehensible numbers of people has been one of our greatest fears, and certainly is now. But this book is not about the infectious diseases on which the popular media have

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focused. It is not about the infectious threats to the rich countries from the poor countries of the world – the Ebola and West Nile viruses that captured headlines, are in fact minor threats. The balance of evidence indicates that the major infectious plagues are not emerging from an African jungle. They are already here, embedded in every society, in rich and poor countries alike. In fact, they have been here for centuries, even millennia. They are as deadly and painful as the sensationalized plagues, but they have spread more insidiously and imperceptibly – they are slow-motion plagues that are difficult to recognize and difficult to control. The flash-fire outbreaks that make the headlines usually burn out on their own. The serious infectious plagues aren't so easy to escape.”

What Dr. Ewald is referring to are chronic diseases.

What if Ewald is right, that chronic diseases have an infectious etiology? The definition of etiology is "the cause, set of causes, or manner of causation of a disease or condition." But it is a chronic etiology – a smoldering – not a raging fire – making the association between disease and infection not quite so obvious, but still easy to prove through appropriate labs tests that are widely available but seldom obtained.

Consider this case study of a 57-year-old manager who had a family history of early death from heart disease. He saw his doctor, and like most healthy people, his LDL was above the standard of care reference range. He was placed on a statin drug, and over the next 10 years, his “total cholesterol” never exceeded 180 mg/dL and most of the time was below 160 mg/dL with his LDL being below 70 most of the time. He achieved the treatment goal of the American College of Cardiology.

Ten years into statin treatment he had a massive heart attack and nearly died. His doctor and cardiologist put him on blood thinners, metformin, and increased the dose of statin. When our manager was admitted to the hospital for the heart attack, blood was drawn. His lipids were “normal” but his white blood cell count was 14,000. White blood cells are part of the innate immune system whereas lipids are not, at least directly. The only conclusion to be drawn is, at the time of the heart attack, he had a pretty strong infection that his immune system was fighting. This fact was ignored as was an appropriate treatment protocol for the highly elevated white blood cells.

Dr. Ewald would argue that, instead of focusing on cholesterol, this person actually had a chronic infection that went undetected for years, leading up to the big event. The problem in identifying this, is that the current standard of care for laboratory values is only looking for what Ewald describes as the flash-fire events, not the subtlety of smolder disease cause by infection.

What caused the manager's heart attack? Infection. He had a history of poor oral hygiene, gingivitis, and root canals that harbor pathogenic bacteria. Not coincidentally, the massive heart attack occurred 3 weeks after major dental surgery

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where his entire upper teeth were removed in preparation for a denture. The dentist, for some reason, did not protect him with antibiotic cover before, during, or after the procedure. Ripping out teeth, which is what was done, is like hitting a hornet nest. Any infection will go scurrying in any and all directions.

The scientific literature has an impressive number of peer-reviewed publications that, if read and the ideas implemented, could have prevented this heart attack. Here are some titles that explain what really happened to this manager.

“Invasive Dental Treatment and Risk for Vascular Events.”⁴⁸ “The rate of vascular events significantly increased in the first 4 weeks after invasive dental treatment and gradually returned to the baseline rate within 6 months.” This is stunning information. A large release of infection takes our immune system and detoxification pathways 6 months to mop up.

“Morbidity and Mortality Associated with Dental Extraction Before Cardia Operation.”⁴⁹ “Patients with planned dental extraction before cardiac operation are at risk for major adverse outcomes, including a 3% risk of death before cardiac operation and an 8% risk of a major adverse outcome.”

“Evaluation of Cardiac Risk in Dental Patients.”⁵⁰ “Patients with cardiac disease, cardiac symptoms and related co-morbidities are increasingly being encountered in dental practice. Current methods of medical risk assessment can however be problematic. This paper represents a multi-specialty consensus on how to identify patients that may be more at risk of an adverse cardiac event occurring peri-operatively i.e. during or in the first few weeks after a dental procedure.”

The manager called the dentist after being informed about the well-studied association between cardiovascular events and oral surgery for infected teeth. The dentist denied that this connection exists. He clearly does not stay current with the literature. The last article cited above is published in British Dental Journal.

An important peer-reviewed paper to read is titled, “The Cytokine Storm and Pre-Cytokine Storm Status in COVID-19. A Model for Managing Population risk for Pandemics and Chronic Diseases.”⁵¹ The lengthy title has a simple translation.

Chronic diseases, also called co-morbidities, drive up death rates from COVID-19.

Cytokines storms are reported to be the killers in COVID-19. A basic definition of cytokine storm is rampant inflammation. Therefore, your pre-existing burden of these cytokines, your “pre-cytokine storm” levels, are a good measure of your risk of dying or having a very adverse outcome from COVID-19. A way to objectively measure the impact of co-morbidities on a person’s health is to analyze biomarkers that quantify the cytokine storm.

This important paper also states,

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"Cytokine storms occur in various illnesses. Bacterial infections that are severe and systemic, causing sepsis, for example, may trigger a storm leading to cardiovascular system failure. Elevated cytokines are present in cardiovascular diseases."

In the Jupiter study, the meager benefit of statin drugs to prevent myocardial infarction was attributed to their action on inflammation as measured by C-reactive protein.⁵² In fact, the anti-inflammatory action of statins may be due to the documented antimicrobial action of these drugs.⁵³ Cytokine storms follow tooth extractions. Dentoalveolar surgical procedures in inflamed and hyper-vascularized tissues could lead to an excessive cytokine release into the blood resulting in unexpected fever, hypotension, dizziness, or death."⁵⁴

This paper took an interesting approach to demonstrating the relationship between chronic infection and chronic diseases. The authors performed a search in the NLM PubMed database for an association between infection and various chronic diseases. Figure 3.1 shows their findings. There is a remarkable correlation between the level of COVID-19 deaths, pre-existing chronic diseases, and the number of research articles connecting the chronic conditions to infections.

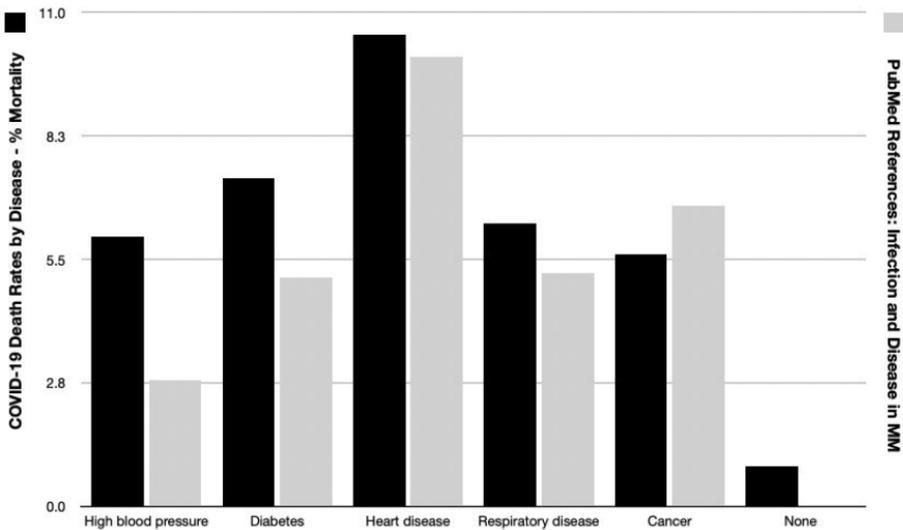


Figure 3.1: Mortality rate for COVID-19 with pre-existing disease by percent (black) and number of references in PubMed with an association between the disease and the term “infection” (grey).

Figure 3.1 shows associations only. However, the number of research articles showing the association between infection and specific chronic diseases is over 1,000,000 in each instance. The association must be considered robust. The way to provide further evidence for this association is through testing. However, this data is unavailable since people with chronic diseases are seldom tested for chronic infection.

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The manager case study and the information provided in Figure 3.1 are extremely important. They point to the mismanagement of patients in our current medical system. It is actually quite simple to explain why the standard of care does not improve health. It seldom considers the action of the immune system. And when it is considered, the interpretation of the information is not science-based and mostly incorrect, as explained in the next chapter. The process of how most chronic diseases develop is straightforward.

- Infections cause an immune response.
- Large segments of the global population are malnourished and have weak immune systems. This does NOT mean people are underfed.
- Infection, when it evades or overwhelms a weak immune system, causes disease.
- Current medical practice does not focus on guiding nutrition and immune support.
- Chronic infections are not considered in most instances of disease.

The medical community focuses on markers like cholesterol that have little or no relevance to infection, immune response, and chronic diseases in particular.

Deficiencies and Immunity

Immune system markers are elevated in essentially all these diseases. Traditional doctors obtain immune response markers like white blood cells, but they emphasize "cholesterol" results much more. The proper treatment approach must focus on the immune response by first finding out what is causing its activation and treating it. Nutrients power the immune system. We must ensure nutrients are "topped off" in our supplies tank to keep immunity running optimally.

The Harvard School of Public Health is an excellent source of nutritional information. An article from this branch of Harvard University titled "Nutrition and Immunity" highlight the relationship between deficiencies and immune system activity.⁵⁵ Key excerpts from the article are included here.

"During the flu season or times of illness, people often seek special foods or vitamin supplements believed to boost immunity. Vitamin C and foods like citrus fruits, chicken soup, and tea with honey are popular examples. Yet the design of our immune system is complex and influenced by an ideal balance of many factors, not just diet, and especially not by any specific food or nutrient. However, a balanced diet consisting of a range of vitamins and minerals and healthy lifestyle factors like adequate sleep, exercise, and low stress most effectively primes the body to fight infection and disease."

"Eating enough nutrients as part of a varied diet is required for the health and function of all cells, including immune cells. Certain dietary patterns may better prepare the body for microbial attacks and excess inflammation, but individual foods are unlikely to offer special protection. Each stage of

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the body's immune response relies on the presence of many micronutrients. Examples of nutrients that have been identified as critical for the growth and function of immune cells include vitamin C, vitamin D, zinc, selenium, iron, and protein (including the amino acid glutamine). They are found in a variety of plant and animal foods."

"A deficiency of single nutrients can alter the body's immune response. Animal studies have found that deficiencies in zinc, selenium, iron, copper, folic acid, and vitamins A, B6, C, D, and E can alter immune responses. These nutrients help the immune system in several ways: working as an antioxidant to protect healthy cells, supporting the growth and activity of immune cells, and producing antibodies. Epidemiological studies find that poorly nourished people are at greater risk of bacterial, viral, and other infections."

"Diets that are limited in variety and lower in nutrients, such as consisting primarily of ultra-processed foods and lacking in minimally processed foods, can negatively affect a healthy immune system. It is also believed that a Western diet high in refined sugar and red meat and low in fruits and vegetables can promote disturbances in healthy intestinal microorganisms, resulting in chronic inflammation of the gut and associated suppressed immunity."

"Eating a good quality diet, as depicted by the Healthy Eating Plate, can prevent deficiencies in these nutrients. However, there are certain populations and situations in which one cannot always eat a variety of nutritious foods or who have increased nutrient needs. In these cases, a vitamin and mineral supplement may help to fill nutritional gaps. Studies have shown that vitamin supplementation can improve immune responses in these groups. Low-income households, pregnant and lactating women, infants and toddlers, and the critically ill are examples of groups at risk."

Importantly, no mention of a drug that improves immunity is in the Harvard School of Public Health article.

How Your Immune System Works

Understanding how your immune system works is the first step to knowing and demanding what tests should be performed to provide guidance on how correct health problems at the root-cause.

What is our immune system protecting us from? According to the CDC, we are under assault from a wide variety of pathogens including: >200 viruses, > 500 bacteria, > 300 fungi, > 250 worms and > 50 parasitic protozoa.⁵⁶ This is just a list of those classified as "pathogens." Each class includes many more organisms that are benign or even beneficial.

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Our immune system is not just a collection of cells and molecules that kill these pathogens. It also plays a major role in promoting the normal functioning of the body, including tissue cleanup and wound repair. Thus, our immune system is also a janitor and nurse. It removes abnormal cells including malignant ones. Immunity is well known to identify and destroy infections goes to extraordinary measures to achieve that goal. For example, certain cells will kill one of our own cells in the process of exposing stealth infection so other immune cells can then eliminate the threat. They are kamikaze cells.

Innate Immunity

Our innate immunity lies in waiting when a pathogen evades our barrier immunity and enters our body.

Innate immunity is the second-line defense from pathogens that try to enter our bodies. This defense is well understood, whereas barrier immunity, the actual first line of immunity defense, is only sometimes considered. The word “innate” is made up of two words, "in" and "nate." “In” means inside, and “nate” means born. Thus, innate is something with which we are born. It is called innate immunity because it is present in our body from the time we are born. Compare this to adaptive immunity that develops after we are born. The innate immune system is an older evolutionary defense strategy than adaptive immunity. Innate immunity is nonspecific, meaning it does not have a special mechanism of action for different types of pathogens. It is a generalist and tries to kill anything foreign.

Innate immunity is most associated with white blood cells. However, this is not the complete story. Protective barriers, or "barrier immunity," can be considered part of innate immunity or classified separately. Known components of innate immunity include:

1. Skin that keeps out the majority of pathogens;
2. Mucus and surfaces within the body that trap pathogens;
3. Stomach acid that destroys pathogens;
4. Enzymes in our sweat and tears create anti-bacterial compounds;
5. Immune system cells attack all foreign cells entering the body.

Barrier Immunity

Barrier immunity includes components 1.-4. above. The skin is the human body's largest organ, with an average surface about the size of a table tennis surface. In simple terms, physical barriers prevent pathogens such as bacteria and viruses from entering the body. The skin provides a physical barrier that prevents pathogens from entering your body and affords protection through chemical and biological barriers. Skin cells produce and secrete important antimicrobial proteins that kill the invading microorganisms. It also contains immune cells that help to stop the microbes from invading our bodies.

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Shedding of skin epithelium, also known as desquamation, helps to remove bacteria and other infectious agents that may have adhered to the skin surface. Similar types of barrier immunity are also provided by many other surfaces present inside our body, including the surface lining of our respiratory system, the gastrointestinal system, the genital urinary system, and the surface lining of our nose and pharynx. All these types of surfaces provide a physical barrier that prevents the attack from pathogens. They also provide various chemical antimicrobials that try to stop the invading pathogens at a very early stage.

As an example of barrier immunity, on the surface lining of our respiratory system are small hair-like projections known as respiratory cilia. A special property of the cilia is that they have a particular direction of movement by which they remove any foreign material that may have entered our lungs. These structures provide a strong physical barrier that prevents the buildup of microorganisms and other foreign materials in our lungs. Defects in cilia function are very common in smokers, leading to a higher incidence of chest infections.

The respiratory surface also provides various types of antimicrobial chemicals like surfactants, mucus, and defensins which help to stop the invading microorganisms. Humans produce and swallow 1.5 liters of saliva daily containing these agents. When functioning optimally and without deficiencies, our stomach releases strong acid developing a very low pH that kills most of the microorganisms we invariably ingest while eating or swallowing saliva. The tears in our eyes also contain special antimicrobial proteins like lysozymes that kill many pathogens. The flushing of tears also prevents foreign material from buildup in our eyes. This, too, is barrier immunity.

Innate Immune Cells

The aspect of innate immunity that can be accurately measured and is invaluable at measuring health are the cells that attack all foreign cells entering the body. The immune system protects us from pathogens, and the term "antigen" is often used in its place. Antigen means a toxin or other foreign substance which induces an immune response in the body, especially the production of antibodies. The word "antigen" is a more generalized term than "pathogen."

When the immune system first recognizes invasion by pathogens, it responds to address the problem. A disease state may manifest if an immune response cannot be activated adequately because the pathogen is evasive or becomes overwhelmed by a virulent pathogen. There are cases where an immune response is activated without an obvious threat. Diseases from this process are called auto-immune diseases. However, having an immune response without a cause never occurs and is more of a reflection of our inability to pinpoint the cause(s).

A less common and insidious problem with immunity is when it is not turned off or turned down even when the danger passes. Allergic reactions and harmful inflammation may result. This is particularly common in the brain, where a one-

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time event (insult) like a concussion may lead to a lifetime of inflammatory misery if the fire is not quelled.

The defense system of innate immunity cells consists of various types of white blood cells and the complement system. In military terms, innate immune cells include the army, air force, marines, navy, and supporting casts. The different types of cells in our innate immune system are:

- neutrophils,
- mast cells,
- basophils,
- dendritic cells,
- eosinophils,
- monocytes,
- macrophages, and
- lymphocytes (NK cells or the natural killer cells).

All these cells are types of white blood cells or WBC's also known as leukocytes, with "leuko" meaning "white" and "cytes" meaning "cell." The neutrophils are the most abundant immune cells making up about fifty to sixty percent of the total population of immune cells, and form an essential part of the innate immune response, especially toward bacterial organisms. Phagocytosis is a key term for the action of neutrophils and other types of white blood cells, with "phago" meaning "eating" and "cytosis" meaning "by a cell."

Neutrophils: Within the neutrophils are granules containing various enzymes released to do the dirty work. Neutrophils are mainly found in the blood and are short-lived and highly mobile, as they can enter tissue parts where other cells or molecules cannot. Neutrophils are usually the first cells to respond to any infection or inflammation due to their heightened ability to sense what is circulating around the body. They do this by detecting unique chemical signals released by pathogens and by our body's special signaling cells that tell them the body's health status. Neutrophils destroy pathogens by producing reactive oxygen species.

Eosinophils: These are another type of white blood cell with a similar structure to neutrophils. Eosinophils are a type of disease-fighting white blood cell. Eosinophilia, the elevation of eosinophils, most often indicates a parasitic infection, an allergic reaction, or cancer. You can have high levels of eosinophils in your blood (blood eosinophilia) or tissues at the site of an infection or inflammation (tissue eosinophilia). The nucleus in these cells usually has two lobes. They also contain numerous cellular granules that contain different types of chemicals and enzymes, similar to but different from neutrophils. Eosinophils make up about one to three percent of white blood cells.

Basophils: These cells are the least common white blood cells representing about one-half to one percent of those in circulation. Basophils have a vital role in

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fighting parasitic infections. They play a role in preventing blood clotting as they contain heparin, a naturally occurring anticoagulant that prevents the formation and extension of blood clots. Basophils are involved in both IgE-dependent and -independent allergic inflammation. In IgE-dependent allergic inflammation, basophils are activated by pathogens and IgE stimulation from allergens, causing degranulation and secretion of cytokines.

Mast cells: These are immune cells that reside in the connective tissue and the mucous membranes, like the lining of our respiratory and gastrointestinal systems. Mast cells are associated with wound healing and defense against pathogens and are often elevated with allergy and anaphylaxis. Mast cells also have numerous granules containing abundant amounts of histamine and heparin. Histamine dilates blood vessels which produce the characteristic signs of inflammation, and recruits neutrophils and macrophages. They also help to link innate and adaptive immunity to fight against pathogens.

Monocytes and Macrophages: These cells go together. A monocyte is a type of immune cell made in the bone marrow and travels through the blood to tissues in the body, becoming a macrophage or a dendritic cell. Macrophage, from the Greek word meaning “large eaters,” is a large phagocytic (pathogen-eating) leukocyte (white blood cell) which can move outside of the vascular system by migrating across the walls of blood vessels and enter the areas between the cells in pursuit of invading pathogens.

Macrophages are the "Pacman" of your innate immune system, referring to one of the early popular video games. Macrophages gobble up big pathogens and debris. The binding of bacterial molecules to the receptors on the surface of a macrophage triggers it to engulf and destroy the bacteria through the generation of reactive oxygen species. Pathogens also stimulate the macrophage to produce chemokines which are special signal chemicals that attract other immune cells to the site of infection.

Dendritic cells: These cells are another of the innate immune cells. The word dendrite means branches, and these cells have branch-like projections. Dendritic cells are present in tissues that are in contact with the external environment, such as the skin and inner lining of the nose, lungs, stomach, and intestines. The dendritic cells are a type of antigen-presenting cell. Antigen-presenting cells detect the pathogens and take the ones present on the surface of these pathogens to lymphocytes.

Lymphocytes are cells of adaptive immunity and are described below. The dendritic cells present specific antigens to the lymphocytes, leading to an attack on the pathogen by lymphocytes and the antibodies they produce. Thus, the designation "antigen-presenting cells." Dendritic cells are also known as the Langerhans cells after the scientists who discovered them. Type 1 interferons, secreted mainly by dendritic cells, play a central role in the body's defense against viruses.

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The final cells in the list of innate immunity are the natural killer cells or the NK cells. NK cells are the component of the innate immune system that do not directly attack the invading microbes. Instead, NK cells destroy our own cells that have become defective such as tumor cells or virus-infected cells. The other cells and components of the innate and adaptive immune system attack the exposed pathogenic cells and destroy them.

The complement system: A particular defense mechanism, still part of innate immunity, is known as the complement system. This system is a set of about twenty proteins, which "complement" the action of the antibodies and other cells in destroying pathogens. Specifically, the complement system helps the antibodies and other immune cells destroy the invading microbes. Many species have complement systems, including plants, fishes, and some invertebrates. The basic mechanism of action of the complement system is as follows:

- Whenever a pathogen enters the body, it is recognized by antibodies in our blood.
- The binding of an antibody to the pathogen is the most important factor for activating the complement system.
- After it is activated, a cascade of different complement enzymes acts on the microbe's surface to kill it.

Measuring or screening for your innate immune response is inexpensive. Ask your doctor for a complete blood count with differential (CBC w/ diff.). If they do not order it, go to a lab that allows you to purchase labs without a doctor. There are many such labs in the United States. Below are the key labs that measure innate response. The values given are scientific and optimal, as discussed in subsequent chapters. The standard of care reference ranges are NOT scientific but based on populations. You do NOT want to be compared to other chronically ill people!

Innate immune response biomarkers and their ranges inferring optimal health are:

- White blood cells: < 4200, >5700 cells per mL;
- Neutrophils: <2000, >3000 cells per mL;
- Lymphocytes: <1400 -, >2000 cells per mL;
- Neutrophil-to-Lymphocyte ratio: < 1.1, >1.4;
- Neutrophil percent: >58%, <52%;
- Lymphocyte percent: <38%, >48%;

Adaptive Immunity

Adaptive immunity is a system that learns to recognize an antigen. It is also referred to as acquired or specific immunity. Adaptive immunity is not present at birth and is created in response to exposure to foreign substances. This system adapts to the type of threats we are exposed to when a pathogen evades our first

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and second lines of defense. Cells and organs like the spleen, thymus, bone marrow, and lymph nodes regulate this system.

Adaptive immunity mainly consists of lymphocytes and the antibodies they produce. When a particular pathogen enters our body for the first time, the response of adaptive immunity is minimal as it does not recognize this pathogen. However, this system remembers this exposure and stores an immunological memory of the encounter. Upon subsequent exposures to the same pathogen, there is a more rapid and amplified response. This system sends multiple types of lymphocytes and specific antibodies for that specific pathogen. The system is highly adaptable because once encountered, the immunological memory of that pathogen remains in our system, possibly forever. This "natural immunity" is superior to vaccination. A complete defense system quickly goes to work upon a new invasion by an old pathogen and is adaptable to changes in the pathogen.

The specific lymphocytes of adaptive immunity are the T lymphocytes and the B lymphocytes. Lymphocytes are a subset of leukocytes meaning they are types of white blood cells. The human body has about two trillion lymphocytes constituting 38 - 48 percent of the WBC's in healthy individuals. Their total mass is about the same as the brain or liver. The peripheral blood contains 2 percent circulating lymphocytes while the rest move within the tissue spaces and the lymphatic system. When the percent lymphocyte count is not in this optimal range, it implies an immune response to some infection, often viral. A thorough diagnostic analysis should be conducted to find the reason for ANY abnormal value.

The adaptive immune system is divided into two main types:

- Humoral immunity (relating to body fluids), which are the B lymphocytes, and
- Cellular immunity (relating to cells), which are the T lymphocytes.

The T lymphocytes are divided into two major types.

1. Cytotoxic or killer T cells (CD8 cells) have a major role in killing pathogens by directly interacting with the invading microbes.
2. T helper cells (CD4 cells) have an indirect but crucial role in our immune system. The helper T cells are responsible for the proper functioning of the rest of the immune cells, including their close cousins, the CD8 cells. They secrete large numbers of growth factors and cytokines essential for the maturation of other immune cell types.

One of the deadliest chronic diseases in recent memory is AIDS, or acquired immunodeficiency syndrome, which functions by killing our CD4 T helper cells. These cells decreased so much that it crippled the whole immune system, which became overwhelmed by various infections that do not usually express in a normal healthy person.

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B lymphocytes: These cells are responsible for humoral (body fluid) immunity. The B-lymphocytes produce a special type of protein known as the antibody, which has a y-shaped structure in which the terminal end of the protein is specially designed to recognize and capture antigens present on the surface of bacteria and other pathogens. This happens after the B lymphocytes have previously had their first contact with the pathogen, which leads to an immunological memory stored inside these cells. Upon subsequent encounter with the same pathogen, the B lymphocyte cells produce many antigen-specific antibodies that recognize and capture the invading pathogen.

Previously it was thought that the antibodies do not destroy these invading pathogens by themselves but activate several different mechanisms of our immune system. This is true partly, but Scripps Institute research shows that antibodies produce reactive oxygen species that can kill the pathogen.⁵⁷ However, the antibody is not left alone in the battle. The complement system, and the various types of phagocytic cells, like neutrophils, contribute to eliminating the threat.

One of these B cell antibodies' essential functions is opsonization, which means sugarcoating a pill to make it tastier. When an antibody recognizes a particular pathogen, they attach to it and coat it with many antibodies. This new cell coating signals other immune cells that find the "sugar" coated cell. Therefore, the antibodies mark the pathogens so they can be destroyed by other immune cells like neutrophils that pack the killing action of reactive oxygen species.

Vaccines and Immunity

The COVID-19 shot, this unprecedented vaccine, is now known to provide limited and only short-term protection against the SARS-CoV-2 virus. Also, the difference in mortality between the young and old is substantial. Some reports, based on available mortality data, suggest that the difference is 10,000%. This type of mortality difference is highly unusual and, at the same time, highly informative about how our bodies respond to the virus.

First of all, before the change in the vaccine definition, all vaccines supported adaptive immunity and not innate immunity. Children's ability to neutralize the virus is most likely linked to the fact that they have a strong innate immune response from birth. This is an extremely important facet of immunity that insures humans survive. When born, the infants have not been exposed to many pathogens. Adaptive immunity is all about exposure and then a response that becomes remembered later in life. Since infants do not have this system established yet they, instead, have a much strong innate immune system compared to adults.

An understanding of the status of an infant and child's immune system is well known. There is some suggestion that the rapidity and scale of children's innate immune response might be protective against the initiation of the SARS-CoV-2

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infection. However, in a world focused on the unprecedented vaccine, this is not a popular view. An article titled, "How kids immune system evades COVID"⁵⁸ does a lot of handwaving on this topic. The article appears in the journal "Nature" which is in the top three list of most respected scientific and medical journals. Here are some excerpts and comments on what the experts say.

Quote: Children's untrained immune response seems to be key to eliminating SARS-CoV-2.

Comment: This immediately infers that it is the innate response that is responsible for eliminating the virus.

Quote: Young children account for only a small percentage of COVID-19 infections⁵⁹ — a trend that has puzzled scientists.

Comment: This should not puzzle scientist. It is well known that children have stronger innate immunity compared to adults. And older adults have weaker innate immunity compared to younger adults. However, this being the case, it is a vote against the value of vaccines in COVID-19.

Quote: Another clue that children's response to the virus differs from that of adults is that some children develop COVID-19 symptoms and antibodies specific to SARS-CoV-2 but never test positive for the virus on a standard RT-PCR test. In one study, three children under ten from the same family developed SARS-CoV-2 antibodies³ — and two of them even experienced mild symptoms — but none tested positive on RT-PCR, despite being tested 11 times over 28 days while in close contact with their parents, who had tested positive.

Comment: They are most likely not testing positive because the innate immune system did not allow the virus to multiply in sufficient quantities to meet the threshold detection limit of the PCR test. This is an elegant, but incomplete, study. They are desperately looking to understand the adaptive immune response difference between adults and children but are not measuring the innate immune response difference. Innate immunity differences are hard to measure using the lab reference ranges of the standard of care (see Chapter 4). They are missing at least half of the information to draw appropriate conclusions.

Quote: Even in children who experienced the severe but rare complication called multisystem inflammatory syndrome in response to SARS-CoV-2 infection, studies report that the rate of positive results on RT-PCR range from just 29% to 50%.

Comment: More proof that the virus is not replicating wildly in children. The negative PCR test infers low viral burden, thus low antibody counts, because they do not have the ability to make antibodies like adults. Their innate immunity takes care of the situation.

Quote: Children's ability to neutralize the virus might also be linked to the fact that they have a strong innate immune response from birth, says Alasdair Munro,

who studies pediatric infectious diseases at University Hospital Southampton, UK. “There’s been some suggestion that the rapidity and scale of their innate immune response might be protective against the initiation of infection,” he says. “But this effect is difficult to study, and raises the question of why it isn’t seen with other viruses that can cause severe disease in children,” he says.

Comment: Dr. Munro is not afraid to go against the vaccine movement and use basic immunology concepts to determine what is going on in the young.

Understanding how our bodies respond to a disease determines how best to survive that disease. Comparing mortality and disease severity between the very young, adults, and older people provides important information on what parts of our immune system are working well or failing. Immunosenescence is a process of immune dysfunction that occurs with age, leading to changes in the immune function of the elderly. The immunity changes track with development of infections, chronic conditions, autoimmune diseases, and malignant tumors. Aiello et. al. explains, “The general picture of innate immunity in older people, which emerges from several studies, is that of the down-regulation of some functions.”⁶⁰

Comparing mortality data on the seasonal flu and COVID-19 is illuminating, Figure 3.2. Innate immunity is strongest in the young an experience a slow decline with age. In old age, innate immunity dissipates precipitously, following a log-linear deterioration.

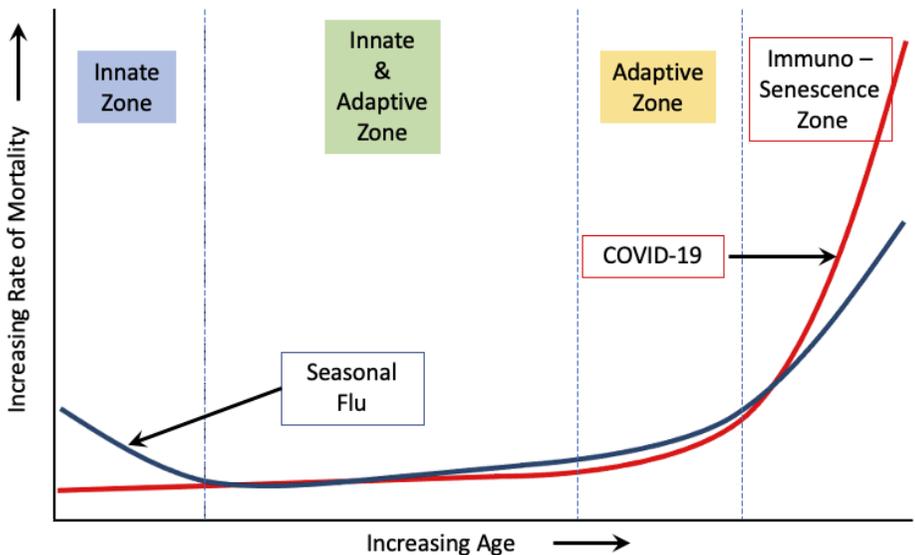


Figure 3.2. Innate immunity is strongest in the young an experience a slow decline with age. In old age, innate immunity dissipates precipitously, following a log-linear deterioration.

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Everyone, regardless of age, has innate and adaptive immunity. The extremes of age are where individuals express the greatest variance between these two types of immunity. How a person responds to infections, with age, provides clues about what type of immunity is most protective.

Deaths and hospitalization rates in the younger population is dramatically lower when comparing COVID-19 and the seasonal flu. The opposite trend is seen in the elderly population, who experience much higher death rates from COVID-19 compared to the flu. These two facts, taken together, provide evidence that innate immunity is much more important in COVID-19 compared to the flu. In the case of the flu, a safe and effective vaccine is an appropriate mitigation strategy, if one actually existed. However, in the case of COVID-19, a vaccine strategy is NOT of paramount importance. Improving health and innate immune response IS the most important approach to reducing hospitalizations and deaths from COVID-19.

Barrier, innate, and adaptive immunity are the primary types of immunity but there are other responses that support these main functions.

Cholesterol

Cholesterol is the most vilified of all substances the body produces yet is actually one of the most important.^{61,62,63} Figure 3.3 shows the change in understanding of cholesterol and healthy fats from the 1960s through today.



Figure 3.3: The change in understanding of cholesterol and healthy fats from the 1960s through today.

Cholesterol plays a role in forming and maintaining cell membranes and structures. Cholesterol can insert between fat molecules making up the cell, making the membrane more fluid. Cells also need cholesterol to help them adjust to changes in temperature.

Cholesterol is essential for making a number of critical hormones, including the stress hormone cortisol. Cholesterol is also used to make sex hormones

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testosterone, progesterone, and estrogen. The liver also uses cholesterol to make bile, a fluid that plays a vital role in the processing and digestion of fats.

Cholesterol is used by nerve cells for insulation.

Your body also needs cholesterol to make vitamin D. In the presence of sunlight, cholesterol is converted into vitamin D. High levels of cholesterol were shown to reduce mortality in AIDS patients.⁶⁴

Cholesterol is a natural antibiotic.⁶⁵

Cholesterol, when allowed to reach a natural level, as governed by our body, is an extremely important part of our immune response.^{66,67,68} New research is showing that cholesterol, when it is too low, substantially increases the risk of cancer or dying from a violent death like suicide.⁶⁹ Did you know that twenty-five percent (25%) of the cholesterol in body is in the brain and that brain is only 2.5% the mass of our body? Therefore, 1000 percent more cholesterol is in brains compared to other body tissue. The level of cholesterol is also very high in brains of other mammals. Finally, the brain is so dependent upon cholesterol that it does not rely on food or the liver as its sole source. The brain makes its own cholesterol.

"Cholesterol Metabolism in the Brain and Its Association with Parkinson's Disease," a research paper described how important cholesterol is to maintaining brain health.⁷⁰ Here is the abstract.

"The brain contains the highest level of cholesterol in the body and abnormal cholesterol metabolism links to many neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis. The blood brain barrier effectively prevents uptake of lipoprotein-bound cholesterol from blood circulation. Accordingly, cholesterol level in the brain is independent from that in peripheral tissues."

Cholesterol is in our body and brain for the good reasons explained here. Part of immunity is the repair of the damage created by pathogens and the cholesterol molecule performs that function superbly. Every cell in the body is composed of phospholipid bilayers. Cholesterol is the key lipid with a concentration of greater than 20 percent by weight in the cells of essentially all organisms with cells.⁷¹

Being against cholesterol is the same as being against a cell!

Amyloids

These formations, like cholesterol, are incorrectly considered toxic to our bodies. Amyloidosis is considered a disease of abnormal proteins - proteins formed in a 'so-called' misfolded conformation. But are they really abnormal or an appropriate response? Amyloids are formed naturally in our body and do not come from the outside like an infection or heavy metal toxin. WebMD calls amyloidosis "a serious health problem that can lead to life-threatening organ failure."⁷²

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Sources like Mayo Clinic claim, “Amyloidosis is a rare disease that occurs when a substance called amyloid builds up in your organs.”⁷³ Are they right or just professing the current dogma?

Beta-amyloid, a type of amyloid formation, is the main “villain” of Alzheimer’s disease. After hundreds of clinical trials that successfully reduced the level of beta-amyloid, and nearly \$1 trillion dollars spent, not one study participant with Alzheimer’s showed any improvement.⁷⁴ These Alzheimer’s amyloid plaques may actually be part of the immune system, an important study revealed. The research carried out at Harvard Medical School indicates that amyloid-beta may be the ‘first line of defense’ against infection in the brain and other tissues.^{75 76} The Harvard team reports, “Members of this evolutionarily ancient family of proteins, collectively known as antimicrobial peptides (AMPs), share many of the amyloid’s purportedly abnormal activities.”⁷⁷

Research Translation: Amyloids are a natural response by our immune system against infection.

Individuals with severe, chronic inflammatory conditions lasting several years deposit amyloid in many tissues and this is a fairly common situation despite prevailing beliefs. Cataract, a very common eye condition, and the most performed surgery throughout the world is an example of amyloid formation.

In Figure 3.4, note the white formation in the center of the eye of this 5-year-old child. She was infected with Ebola and survived. A natural response to the disease is an amyloid formation that is commonly called a cataract. Research from Harvard Medical School published in 2003 shows that cataracts are a type of amyloid and they actually form to protect the eye from infection.^{78,79} It is highly likely that this child has amyloid formations throughout her body.



Figure 3.4: Nuclear cataract in a 5-year-old girl infected with Ebola. Prior to the infection, then lens in her eye was cataract-free.

Cataracts are common in older people without Ebola infection. What they have instead is a chronic condition stimulated by a chronic infection. Cataract sufferers

do not know they have a chronic infection because it causes a mild and localized effect in the eye. The infection may be more widespread, but the eye is transparent, and the amyloid formation is easily observed. People with cataracts die young compared to similar people without cataracts, indicating that, most of the time, the infection has an impact beyond the eye.⁸⁰

This peer-reviewed information indicates that amyloid and other substances that are not well understood but produced by our body mount a natural protective response to disease by responding to chronic infections.⁸¹

The common thread between all the immune cells of innate, adaptive systems and amyloidosis, which could be classified as a secondary immune response, is that they primarily defend against infection. Is modern medicine looking at the wrong disease-causing culprits?

According to Dr. Ewald, Evolutionary Biologist,

“The textbooks say, in 1900, most people died of infectious diseases, and today most people don't die of infectious disease; they die of cancer and heart disease and Alzheimer's and all these things. Well, in time, I think the textbooks will have to be rewritten to say, ‘Throughout history, most people have died of infectious disease, and most people continue to die of infectious disease.’”⁸²

Evasive Pathogens

Microbes can evade your immune system. For example, salmonella, which causes food poisoning, and mycobacterium tuberculosis are quite evasive. Streptococcus pneumoniae is an example of a bacterium that changes its outer surface to make antibodies less protective against reinfection. Vaccines for this disease have 23 different variants and are not very effective because this organism can morph and hide. Influenza and the common cold have so many variants that the adaptive immune system may never have all of them in its catalog of causal agents. Notice there is no vaccine for colds. Thus, you may still get the cold or flu when you are 100 years old. Modern medicine cannot keep up with the morphing of flu variants.

The flu vaccine has marginal efficacy because the organism causing the disease changes to avoid the immune system and vaccines.

In 2019, the CDC reported that the season's flu shot was only a 45% effect which was an improvement over 2018. Of course, they still recommended the shot. They gave little advice on how to boost immunity to reduce the severity of the flu and only provide annual recommendations for a relatively ineffective vaccine. The exact quote from the CDC website reads,⁸³

"According to data from the U.S. Influenza Vaccine Effectiveness Network on 4,112 children and adults with acute respiratory illness from October 23, 2019 - January 25, 2020, the overall estimated effectiveness of seasonal

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influenza vaccine for preventing medically attended, laboratory-confirmed influenza virus infection was 45%."

The term "effectiveness" is not defined.

Most studies indicate that the flu, or other evasive pathogens, do so by creating variants. But that is not the only way an infection can evade the immune system. Consider an emerging concept referred to as infectogenomics. Kellam et al., in their article titled "Infectogenomics: insights from the Host Genome into Infectious Disease," provide some thoughtful insights.⁸⁴

"As with most biological phenomena, the disease is the outcome of both nature and nurture. In the case of infectious disease, however, the interaction of two natures, that is, two genomes (host and pathogen), is at play. Environmental and social factors, or nurture, may affect the risk of acquiring infection and also the risk of becoming ill. How we behave and our environment will determine the number of exposure events. The dose of infection and the fitness of the host and pathogen will determine sickness."

Minarovits, in a paper titled "Microbe-induced epigenetic alterations in host cells: the coming era of patho-epigenetics of microbial infections," suggested that we have significant challenges when avoiding disease from pathogens.⁸⁵ This statement accounts for why sixty percent of American adults have at least one chronic disease. His language is highly technical, thus this translation:

- The genetics of microbes may interact with the genetics of the host (you), creating epigenetic changes.
- The pathogen does this to create epigenetic dysregulation and subsequent cellular dysfunctions that may lead to disease.
- The author proposes that pathogens may induce pathological changes through the "epigenetic reprogramming" of specific cells.
- This entire process ensures the survival of the pathogen.

In other words, the pathogen may be able to change the way your immune system responds to it as a survival mechanism. But do not be dismayed because epigenetic processes can be reversed. Elimination of the offending microbes that have the potential to reprogram cell genetics is the first step towards preventing disease development and reversing disease. The primary approach, even before pathogen elimination, is building a strong immune system to curb the growth of pathogens.

Back to Kellam:

"In studying the severity of infectious diseases, it is not always clear how much variation to attribute to the virulence of the pathogen and how much to the susceptibility of the host. In some situations, however, the pathogen can be regarded as a constant (meaning - the microbe has the same

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pathogenic impact regardless of who is infected), thereby revealing the contribution of the host.”

This last statement clarifies the importance of our immune system in dictating disease severity.

You have control over our outcomes – most of the time.

What can you do? Never let down your guard. Measure, and optimize your immunity. It is the weapon over which you have control.

Hopefully, these examples heighten your awareness of the action of your immune system. Chapter 4 delves into how to correctly measure your immune strength and response. No one has specific immune functions to fight heart disease, diabetes, Alzheimer’s, mood disorders, and Cancer. Our immune system fights infection.

Infection would be a real and tangible root cause of chronic diseases if only medicine looked for it. Is a calcified vessel really a root cause? Do you really have a statin deficiency? If you are acutely or chronically ill, your immune system activity tells the story of how it is protecting you from infection. Measure it regularly and take action to enhance its capability.

When the Immune System Redlines

The COVID pandemic has acquainted the world with the term "cytokine storm." Many COVID-19 complications may be caused by a condition known as cytokine release syndrome or a cytokine storm. This is when an infection triggers the immune system to flood the bloodstream with inflammatory cytokine proteins. They can kill tissue and damage organs while working to eliminate an infection. The dose makes the poison. Cytokine storms are not exclusive to COVID-19. The most recognizable condition of a cytokine storm is sepsis.

A group out of Australia studied “perpetual inflammation” in the brain. They argue that mild cytokine storms cause many brain ailments, but these low-level continuous storms are not common outside the brain. Their summary paper is titled “The meteorology of cytokine storms and the clinical usefulness of this knowledge.”⁸⁶ The number of new papers that cite this work is a meager 64, indicating that few in the medical community are paying attention to this topic. Their pithy explanation of perpetual inflammation, particularly in a low-grade form, is instructive in understanding unrelenting brain and mood disorders. This excerpt, modified slightly for clarity, explains that brain disorders are not “all in your head.” Instead, there is a persistent immune response in the brain that actually impedes recovery.

"Moderate but persistent cytokine storms are typical of chronic neurodegenerative states, including post-stroke, post-traumatic brain injury, and Alzheimer’s disease (AD). In the weather analogy, cytokines

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are what water is to life. Light falls of rain and low levels of inflammation keep physiology ticking over an organism's life."

- Crops grow in moderate amounts of rain, and self-limiting innate immunity cures.
- Both rain and cytokines can kill in acute excess or unrelenting moderate amounts.
- Both the acute and unrelenting patterns are valid cytokine storms.
- When excess cytokine is generated within the brain, the result is non-resolving inflammation.

Inflammation is a signal that our innate immune system is working. So why does this impede healing? A Stanford Medical School team explains this issue in a paper titled "Inflammatory blockade restores adult hippocampal neurogenesis."⁸⁷ This article is cited over 2,500 times. Thus, there has been a tremendous body of literature related to this topic since its publication. Just dissecting the title provides all that is needed to understand why perpetual inflammation causes disease. Here is a translation of the title.

Inflammatory blockade = Stopping inflammation.

Hippocampal = Part of the brain, in particular, the gray matter that has a central role in memory processes.

Neurogenesis = Birth of neurons

The title, in laypersons terms, is:

Stopping inflammation (including its causes) leads to the birth of new neurons and restoring brain function and memory.

The brain is not completely unique compared to tissue elsewhere in the body. Chronic conditions like arthritis are also due to low-grade inflammatory processes. However, the difference is, in the brain, inflammation seems to be able to perpetuate even when the causes - the trauma or infection - are long gone.

Vaccines & Liability

Merck settled Vioxx lawsuits for \$4.85 billion. The death toll from this drug, which passed five years of safety studies, exceeded 50,000 people, with some estimates as high as 500,000. Drugs and medicines are frequently at the center of product liability suits. Manufacturers of these products have a duty to appropriately test the drugs and therapies before releasing them into the market, using testing criteria from the U.S. Food and Drug Administration (FDA). These criteria are regarded as industry standards, but the fact that the FDA properly licensed a drug does not affect the manufacturer's liability to an injured plaintiff if the drug proves to be otherwise defective. Sadly, drug companies are not liable for defective vaccines.

Chapter 3. What is Immunity

Potential liability for vaccine-related injuries has received much attention as a deterrent to vaccine manufacturing. Under 42 U.S. Code § 300aa-22 - Standards of responsibility,

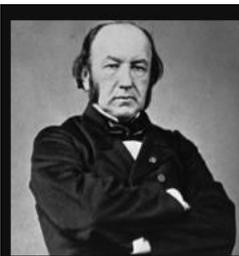
"No vaccine manufacturer shall be liable in a civil action for damages arising from a vaccine-related injury or death associated with the administration of a vaccine after October 1, 1988, if the injury or death resulted from side effects that were unavoidable even though the vaccine was properly prepared and was accompanied by proper directions and warnings."

What is the incentive to thoroughly test vaccines for safety if there is no financial risk to the manufacturer?

If truly safe and effective, vaccines are a viable technology to reduce infectious diseases in populations, but it is only part of the story. Vaccines support adaptive immunity, not innate immunity. Both aspects of immunity are critical to curbing diseases. Why was the vaccine the only narrative during the COVID-19 pandemic? The simple answer is that modern medicine does nothing to support innate immunity.

The only drugs supporting innate immunity are anti-infectives like antibiotics and Ivermectin. For example, most anti-inflammatories used in modern medicine suppress rather than augment immunity. None of these directly foster improvements to innate immunity, but they do reduce the amount of infection that requires an immune response. However, natural substances containing high nutrient density and specific infection-fighting substances like vitamins A and D do.

The COVID-19 pandemic hopefully turns into a learning experience where true science prevails. Analyzing data on death and hospitalization rates for influenza compared to COVID-19 provides a sound foundation for the immune mechanisms activated in each case. That deaths in the young are much higher in influenza should signal to anyone with basic knowledge of immunity that innate immunity is more important in COVID-19 compared to Influenza. This fact should drive health policy toward good health, not treatments. Politics and profits must leave medical decision-making. Verifiable data must be the policy driver even when it is unpopular.



The experimenter who does not know what he is looking for will not understand what he finds.

~ Claude Bernard

Chapter 3. What is Immunity

The quote by Dr. Bernard below is a reminder that infection is the root cause of most chronic diseases. This is well-known but ignored because it is an inconvenient truth.

Review

Barrier Immunity: Barrier immunity is part of innate immunity and includes several organs and tissue, the first being the skin. Similar types of barrier immunity are also provided by many other surfaces present inside our body, including the surface lining of our respiratory system, the gastrointestinal system, the genital, and urinary systems, and the surface lining of our nose and pharynx.

Innate Immunity: We are born with this non-specific immunity that rapidly reacts to invaders and kills a wide range of pathogens.

Adaptive Immunity: This immunity is acquired over time by exposure to environmental pathogens. The adaptive immune system is slower to respond compared to innate immunity, as it needs the first exposure to develop a memory of the pathogen. The key cells of adaptive immunity are lymphocytes.

Vaccines are intended to boost adaptive immunity and have no direct impact on innate immunity.

Secondary Immunity: This is a vast and mostly unexplored part of immunity. Cholesterol and amyloid formations are part of this system.

Your immune system is always working to keep you healthy and alive. The immune response is often demonized through the term "inflammation," However, inflammation is an indication that your immune system is at work. Also, the immune response is viewed as an off-or-on switch by most doctors. However, this is a naïve view. The next chapter explores how to properly measure the activity of the innate immune system as the most important step in measuring health and chronic disease burden and what to do about it.

Chapter 4. Health is a Continuum

No one is either healthy or sick. Instead, we all reside on a health-disease continuum.

- Thomas J. Lewis, Ph.D.

Health is a Continuum

In traditional medicine, you are either healthy or sick. How many people are dismissed when they go to the doctor with health complaints? "It is all in your head" is often concluded by providers in this system. There are three reasons for this.

1. The lab "normal" values imposed on doctors are inaccurate or insufficiently sensitive to determine if you have a chronic condition. Even when you are ill, your labs often appear normal.
2. To do something to "manage" your symptoms and get paid for doing so, your doctor must assign a diagnostic code. If your symptoms do not match a code, your problem goes unheeded.
3. Regardless, the doctor never searches for root causes and only addresses reducing symptoms with drugs or procedures. Unfortunately, this approach usually results in even more symptoms and more drugs.

The standard of care perpetuates poor health.

We are NOT either healthy or sick. Instead, we all lie on a health-disease continuum. Most of us prefer to prevent a diagnosis rather than "treat" the symptoms. In this continuum model, however, there is no such thing as prevention. Instead, through proper measurement and concomitant actions, people can stave off or reverse a diagnosis on their way to more optimal health along their health continuum. Therefore, this approach is not about prevention. Instead, it is an optimization method for everyone, including those with illness and those who are "apparently" well. No one has perfect health.

"We ignored the science, and patients paid the price with their lives."

- Peter Pronovost, M.D., Ph.D., a patient-safety expert and a professor of anesthesiology, critical care medicine, and surgery at the Johns Hopkins University School of Medicine.

Health freedom is lost because the medical industrial complex uses archaic and inadequate analytics to measure your health. Without good measurements, you

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cannot get appropriate and effective treatment. As a result, you do NOT have healthy freedom of either knowledge or choice.

Typically, your health is measured with “labs,” also known as biomarkers. Two necessary overhauls to the existing system are essential to reestablishing the healthcare system instead of perpetuating our "sick care" system. These two are changing the depth and breadth of biomarkers obtained for everyone. Unfortunately, the current complex medical infrastructure may never cede to this change. Therefore, we must replace this system. There is no option 2 involving a compromise.

In health, making compromises is unacceptable.

Overhaul 1. Depth of Biomarkers: Completely change reference ranges for lab “normal” values from unscientific population-based to science-based and data-driven values. Smoldering chronic diseases are the most prolific, and lab values associated with these conditions seldom exceed reference ranges.

Overhaul 2. The breadth of Biomarkers: Completely change the labs routinely drawn on everyone. The routine standard panel must be a new and broader set of biomarkers substantially more predictive of your future health.

When combined, a broad and deep health assessment, with labs as a cornerstone, constitutes a revolutionary change compared to the current "garbage in - garbage out" process. The ultimate outcome of this approach to lab interpretation is the recognition that every one of us has different health risks. Notably, chronic diseases smolder, often for decades, before disease suddenly erupts. Yet, this concept is completely ignored in the standard of care.

We all reside somewhere on a health-disease continuum, Figure 4.1. Overhauls 1. and 2., when implemented, accurately place individuals on the continuum. Showing where people reside on the continuum creates a sense of urgency as many who presumed they were in perfect health find out they are not. Precisely understanding your health most likely leads to implementing protocols driven by the new abnormal values.

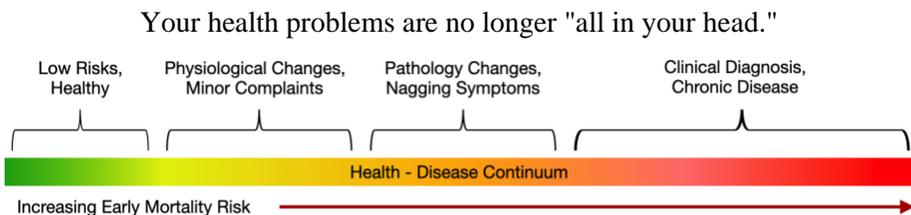


Figure 4.1: Health-disease continuum based on risk and biomarker scoring using science-based measurements.

Improving diagnostics and interventions will lead to a shift to a healthier population. Regrettably, the current system has and will continue to lead to a shift

Chapter 4. Health is a Continuum

to a less healthy population. If your doctor tells you, “You are fine,” there is nothing to do. However, if you are told you may feel well but are on the wrong side of good health, you will be more inclined to take appropriate action.

In most cases, the existing standards for interpreting health, based on biomarker values for labs drawn every day, are outright erroneous. Biomarker measurement is fundamental to objectively measuring health. Markers of basic immunity are the most important to obtain and are essential for illuminating your health status regardless of how well you currently feel. You will only know how truly healthy you are if the suitable biomarkers are measured and interpreted correctly. Symptoms seldom emerge before lab values start increasing. Proper knowledge about your health is the key to unlocking your long-term health freedom.

As a result of health freedom lost, people of the United States, in particular, face a major health crisis. The U.S. healthcare costs are the highest per capita compared to other developed countries by far. In Americans, disease rates are high and longevity low compared to other developed nations. We are in a lose-lose situation. Here is a quote from an NBC News article.⁸⁸

“Americans are below average on most health measures - from obesity to infant mortality - compared with other rich countries, and they're falling behind on lifespan, too, according to the latest survey.”

The annual survey from the Organization for Economic Cooperation and Development (OECD) shows that the U.S. spends far more than any comparable country on health care yet gets far less for its money. As a result, Americans are shorter, fatter, die younger, and do not get particularly good treatments for many diseases.

We must make a revolutionary change to the healthcare system. That change cannot be a few tweaks here and there. That change must be foundational. Specifically, the new system must emphasize the causes of chronic diseases. Even the U.S. CDC acknowledges how prevalent chronic diseases are. Figure 4.2.



Figure 4.2. The CDC explains that most diseases are chronic in nature.

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Here are some high-level concepts for revolutionary change.

Life risks drive disease. Proper healthcare must capture historical and current risks, including each person's subjective health. Risk information must be obtained through a digitized survey instead of being captured in static files so the information can be data-minded to establish risk-disease associations. Our existing sick care system considers a few common risks, and they are only conveying a small portion of our health story

The ultimate objective of a comprehensive risk assessment is not to steal or punish you with higher premiums. Instead, the purpose is to create strong associations between risks and adverse outcomes. Hence, the new healthcare delivery system works with you, using personal and precision medicine to properly prioritize YOUR information. With robust data, no doctor should ever say, "those symptoms are all in your head."

Physiological measurements provide objectivity. If modest risks perpetuate or someone has concerning risks, physiological (biomarker) rise or fall from optimal. Most diseases are chronic and smolder for an extended period before symptoms or disease emerge. Paramount to characterizing and reversing chronic processes is a proper interpretation of labs.

The current reference ranges must be mothballed as they do more to protect doctors from liability than to protect you from progression into severe disease. Longevity is a strong indicator of health span and a strong indicator of health and disease. Not many people live a long unhealthy life. Thus, data on early mortality or survival is a powerful predictor of health. The revolutionary change to the interpretation of labs has to be the cornerstone of health assessments. Scientifically established early mortality risk should become the standard. The current sick care lab values are subjective as opposed to objective.

Pathology assessments offer chronic disease screening. The current system provides a meager level of screening, many of which are rather invasive, thus limiting acceptance. The eye offers a unique window to health. Eye exams are inexpensive and readily available throughout the United States. Optometrists and ophthalmologists are able to perform these tests. The exams are non-invasive and well-tolerated.

Remarkably, eye evaluations can reveal major disease mechanisms, including neurodegeneration, inflammation, vascular disease, and infection. Diabetes shows up in the eye early into the process. Therefore, screening for the earliest pathology changes is critical in creating more impactful health delivery. This approach to early disease detection is crucial in the United States, where healthcare costs drain many Americans' disposable income.

Treatment protocols must be rebuilt. In the current standard of care, the time between a discovery and a change in diagnoses and treatments is far too long. Statin drug use is an example. They provide no benefit based on mortality data,

Chapter 4. Health is a Continuum

but they will probably be prescribed regularly for decades to come. However, cardiovascular disease continues to be the leading cause of death in the developed world. Statins are NOT working, but doctors are not provided with tools and knowledge to understand root causes. Doctors need to be free to be doctors. The static, outdated, ineffectual code book that doctors are forced to use to obtain payment must NOT control tests and interventions. Instead, the codebook must be capable of evolving to accommodate new and better approaches.

Dr. Paul Marik provides a poignant example of how new knowledge is not incorporated into medicine even when it does no harm and is inexpensive. He showed that high doses of vitamin C substantially reduced sepsis mortality rate. These "do no harm" interventions must immediately be made available to doctors through a flexible digitized guidance system - not a rigid coding system. This process of continuous improvement is routinely applied to industries other than healthcare. Instead, the current medical system's "continuous improvement" is new and high-profit drugs that do not afford better outcomes. They often replace off-patent drugs. These older drugs have proven safety profiles, but none afford the outcomes patients want. The current system is continuously improving profits, not health.

So much for the Hippocratic Oath!

The process for qualifying and approving new interventions must be re-engineered. Currently, the "so-called" gold standard for approving new medical interventions is the randomized clinical trial (RCT) process. This system is rigged to only approve expensive new drugs or devices for profit, not health. A substantial body of data shows that we do not need a continual flow of new drugs. More weight needs to be applied to population studies that often demonstrate the value of existing therapies or lack thereof.

An example of an inappropriate approval is statins for cholesterol treatment. RCTs on cholesterol included thousands of study subjects. The data showed meager benefits using absolute as opposed to meaningless relative statistics. However, manipulating the statistics was all it took to convince doctors to put a substantial portion of our population on statins. Population studies on millions of people show that the RCT conclusions about lower cholesterol are entirely wrong. What data would you prefer to have applied to your health?

1. Data from small pharmaceutical company-selected groups? Be aware that the FDA does not require pharmaceutical companies to submit all information obtained in an RCT. So, naturally, they cherry-pick the best data.

OR

2. Information obtained on millions of people like you in a real-world environment.

Disease mechanisms must drive medical interventions. The current diagnostic coding system creates meaningless human-defined syndromes. For example, does "multiple sclerosis" provide any insights into why the disease is occurring? "Multiple" means "many," and "sclerosis" means "abnormal hardening of body tissue." Most of the ~70,000 coded disease labels must be mothballed. Instead, healthcare needs to appreciate and operate with an understanding of disease mechanisms.

Only a few mechanisms are responsible for the major chronic conditions, including cancer, Alzheimer's, diabetes, and heart diseases. You can prove this to yourself by going to the various disease associations or the Mayo Clinic website and searching for their published disease risk factors. The same ones keep showing up over and over again. However, new drugs are continually introduced based on the vast set of diagnostic codes. Is this system working? See figure 4.2.

Five (5) mechanisms explain most diseases' underlying (root-cause) drivers. They are,

1. Poor micronutrient status from poor diets, behaviors, or poor absorption.
2. Thrive vs. survive. In other words, stressors make a person vulnerable to low-grade toxicity or infections.
3. Stealth and chronic infections and toxins, with infections being the greatest offender.
4. Infections, specific sensitivities, and processed foods cause perpetual low-grade inflammation.
5. Lack of autophagy due to a sedentary lifestyle and constant eating.

Certainly, all diseases are not driven solely by these five mechanisms. Thus, others must be determined.

The COVID-19 pandemic provided bona fide evidence that our healthcare system is malfunctioning. Regrettably, the so-called "big data" that has been around in healthcare for decades has contributed no solutions to the pandemic. Big Data is supposed to help healthcare providers by providing new insights into existing health information in unprecedented ways. The potential of big data in healthcare, however, relies on the ability to detect patterns and turn high volumes of data into actionable knowledge for decision- and policymakers while providing more precision to medicine. Thus, big data's non-contribution to the crisis illustrates that it, too, lacks health freedom. The data available to these algorithms is quite "big," but it is hardly good data. The expression "garbage in, garbage out" comes to mind.

The article "Benefits and challenges of Big Data in healthcare: an overview of the European initiatives"⁸⁹ unwittingly explains the limitations of big data. Some key excerpts from this paper include:

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"According to McKinsey, the term Big Data refers to datasets whose size is beyond the ability of typical database software tools to capture, store, manage, and analyze."⁹⁰

"Gartner proposed the popular definition of Big Data with the '3V': Big Data is volume, high-velocity, and high-variety information assets."⁹¹

The concept of "high-variety information assets" is not applied to medicine. For example, the same lipid and metabolic labs are obtained for everyone. These limited tests hardly constitute "high variety."

According to other definitions, "Big Data is also characterized by a fourth dimension: Veracity, concerning the quality, authenticity, and 'trustworthiness' of data."⁹² Unfortunately, the quality, authenticity, and trustworthiness of the medical data used to improve your health are inferior. As a result, payer systems, drug companies, and the FDA use misinformation, not viable data, to rationalize approval of interventions that do not improve your health.

Furthermore, there is an emergent discussion that 'Big' is no longer the defining parameter but rather how 'smart' the data are, focusing on the insights that the volume of data can reasonably provide.⁹³ Deming perfected the process of continuous improvement, which means learning from mistakes and triumphs and evolving. Unfortunately, the coding system restricts doctors, so there is no evolution or advancement in "smart" data.

Doctors are essentially rereading "See Spot Run" rather than advancing to "The Tale of Two Cities." That is, they too often rely on the glossy pharmaceutical brochure rather than delving deep into the medical research literature that does have much of the right information if you know how to filter out the bias. Big data is challenged to build a "bias alert" filter. A recent test of an artificial intelligence system unmistakably demonstrates that it could not solve the most fundamental problem because biased data was used.

The Tale of Two Cities is about revolution, and we need a medical revolution on the scale described in Dicken's book. If Big Data cannot help in a crisis, how can your doctor, who works from a much smaller set of knowledge? In COVID-19, only outliers like Drs. Kory, Zelenko, Kory, Marik, and McCullough, who possess great medical knowledge beyond the standard of care, contributed impactful solutions to the crisis. But, as the story developed, they were either marginalized, ignored, or demonized because what they suggested was viewed as going against the standard of care. The standard of care must take a back seat in a crisis pandemic. Dr. McCullough repeatedly communicated that doing typical trials on novel or existing interventions as if we were not in a crisis was mind-boggling, therefore, most likely agenda-driven.

The Health-Disease Continuum

The coding system has squashed health freedom that most doctors use to get paid for clinical visits. Are we really either healthy or sick, or could we be somewhere in between? People have very different health profiles; thus, obtaining a wide range of biomarkers is absolutely necessary to obtain a proper medical “workup.”

Genetics and Epigenetics

Genes vary by 0.1 percent in humans, but how we live varies by 99.9%. It is quite naïve to have only two classifications. Instead, we all lie on a health-disease continuum. Somewhere in the world is the healthiest person who is or will live close to 120 years of age. Somewhere else is a young person on death’s door. The rest of us lie somewhere in between. These two extremes set the upper and lower limits for the health continuum.

Humans are 99.9% the same genetically, according to the National Institutes for Health (NIH) Human Genome Research Institute.⁹⁴ Humans are also close cousins of other animals, with a genetic material overlap of 96 percent with chimpanzees, 90 percent with cats, and 85 percent with rats. Leave it to the Federal Government to make wrong conclusions as the NIH indicates that the 0.1 percent difference in genetic makeup holds important clues about the causes of disease. They have not studied identical twins' health profiles that share identical genes.

Indeed, there are some rare genetic diseases like Downs Syndrome and Sickle Cell Anemia, and they are sometimes detected at birth or before. The remaining ~70,000 diseases coded in ICD-10 are behavioral and environmental. The many twin studies corroborate this very clearly. However, authors of these studies often confuse genetics for epigenetics when concluding the reason for differences in twins' health. The article “Twins and Cancer: Nature, Nurture, or Something Else?” clarifies the factors impacting disease outcomes.⁹⁵

If genetics controlled your health rather than you controlling your genetics, then many of the tests performed to assess your health and interventions provided to you would be of no real value. This is because even advanced medicine cannot treat your genes but can treat you.

Epigenetics studies how behaviors and the living environment can cause changes that affect how genes work. Unlike genetic changes, epigenetic modifications are reversible and do not change the DNA sequence. However, they can change how the body reads a DNA sequence. This discussion about genes versus epigenetics versus lifestyle and environment is critical. If diseases are primarily tied up in our genes, why make any effort to be healthy? Our genes do NOT dominate diseases; instead, diseases are governed by our situations and behaviors.

Your decisions dictate your health.

Infection can alter the host genome. If the host for infection is one of two twins in the womb, these identical twins are destined to be different and possibly quite

different. No research into twins and health take this into account. Time spent in the womb is considered identical in identical twins. However, this is not likely the case. Take your eyes as an example. Every individual has two eyes. An individual may experience exposure to something harmful, like a pathogen, that leads to an eye disease. Most often, eye disease first impacts just one eye. After that, it may spread to the "fellow" eye but seldom does the condition immediately manifest in both eyes simultaneously.

Paul Kellam and Robin Weiss explain the consequences of infection on the genome in their paper titled "Infectogenomics: insights from the host genome into infectious diseases." Their conclusion is included here.

"The functional genomics of the host is crucial in analyzing host-pathogen interactions. Host genetic variation plays a key role in determining the outcome of many potentially pathogenic infections, and the prevalent pathogens have influenced the genetic makeup of human populations. Infectogenomics can be harnessed to identify infectious states, understand the host response, predict disease outcomes, monitor responses to antimicrobial therapies, and indicate promising new types of treatment.

In addition, we should acknowledge that the disease state can inform our understanding of normality. Just as virology led us to oncogenes, tumor suppressor proteins, membrane trafficking pathways, and other aspects of molecular cell biology in the past, so can studies of the perturbation of the transcriptome by infection open new vistas onto "systems" biology today."

Infections historically are the major cause of disease and early death. However, in the modern era, conditions are not considered to be caused by infection. Instead, tens of thousands of human labels are applied to diseases, including cardiovascular disease, cancer, diabetes, and Alzheimer's disease. Infections of all types illicit a reaction by our immune system that is measurable with biomarkers. In Volume 1, a chapter is devoted to understanding the stealthy but prolific nature of infections in modern diseases.

Measuring biomarkers may be unimportant if diseases were genetic because genes cannot be treated. Fortunately, almost all conditions are treatable and reversible. Thus, measuring biomarkers and applying treatment protocols based on biomarkers and risks remains the single most important way to ensure good health or reverse diseases. Interestingly, the change in biomarkers with stealth, chronic-phase infections is small. Thus, with the current reference ranges not based on science, individuals infected with chronically usually test "normal." Therefore, the person with this condition has a smoldering disease that goes undetected until it suddenly erupts sometime in the future, to the "surprise" of the medical team.

Prevention

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Prevention is a tiny part of current insurance-based medicine. A cured patient is a lost customer. Symptoms and biomarkers are real, but diagnostic labels are artificial human-defined terms. Thus, they are subjective. Importantly, the term prevention is irrelevant within the concept of the health continuum. Since everyone is somewhere on the continuum, the goal of healthcare must be to "slide" everyone to its better side. In that process, the person may transition from a state defined as having a disease to a state of good health where the person is disease, diagnosis, and symptom-free. There is no "prevention" in this process, only improvement.

In the health-disease continuum, model prevention does not apply. Instead, the goal is to move everyone to the healthier side of the continuum.

In the standard of care, there are a few codes for prevention. The codes apply to two categories: routine doctor visits and screening. These preventative routine doctor visits are not new. Doctors have always done annual checkups. Many of the preventative screening codes are a trap to put the unwary patient on a drug or get a procedure. Table 4.1 lists preventative screenings and the most likely outcome from the encounter.

Preventative Screening	Likely Outcome
Cardiovascular screening	Statin, blood pressure, and diabetes drugs
Colorectal cancer screening	Surgery, radiation, and chemotherapy
Depression screening	SSRI drugs
Diabetes screening	Metformin and Insulin
HIV Screening	Antiviral drugs
Lead poisoning screening	Chelation (they got this one right)
Lipoid disorder screening	Statin, blood pressure, and diabetes drugs
Obesity intensive behavioral therapy	Seldom happens
Osteoporosis screening	Bone scan and harmful Fosamax drug
Prostate cancer screening	Surgery, radiation, and chemotherapy
Pulmonary tuberculosis	Antibiotics
Sexually transmitted infection	Antibiotics

Table 4.1. Preventative screenings that are available within the ICD-10 code book and potential treatments for those being screened.

Cardiovascular screening is particularly mismanaged because healthy people frequently have what the standard of care calls "high cholesterol." When evaluating labs, the total cholesterol value is very often abnormal, even in people who are actually quite healthy. Shockingly, they are literally threatened to take a statin drug to "protect your heart." The values the standard of care uses to declare lipids are abnormal are completely wrong. People's health is jeopardized when treatments are prescribed to lower cholesterol values to standard-of-care normal values. See Volume 1 for more details.

Of the two overhauls needed, that is, depth and breadth of biomarkers, “depth” constitutes the most significant needed change. For example, if more biomarkers are added to a panel, but the reference ranges are incorrect, the diagnosis remains inadequate or incorrect.

Overhaul 1. Depth of Biomarkers

Dr. Clement Trempe of Harvard Medical School often started conversations with other doctors, saying, “Are you proud of your workup?” What he meant is, have you done all the proper assessments and diagnostic tests to determine what is causing the ailments presented by your patients? He was the first doctor to explain that reference ranges for biomarkers changed in the wrong direction and were imprecise at measuring health. He also said that early mortality is the most important medical endpoint. Therefore, the most logical science-based reference range for biomarkers is based on widely available early mortality data. As explained in Chapter 1, morbidity (disease) and mortality (dying young) are intimately intertwined. The standard of care reference ranges are not based on sound science like this.

The entire purpose of today’s laboratory reference ranges is to determine if you have a diagnosable medical condition. However, these ranges completely ignore that health and disease are a continuum. Diabetes “happens” when your A1C is 6.5% or above. However, the preferred value for A1C should be close to 4 - 5% to be truly healthy. At <5%, human physiology is complete “insulin sensitive.” That means the hormone insulin is 100% efficient at escorting glucose into a cell that requires energy. Any value above an A1C of 5 percent infers the beginnings of the human-defined disease of type 2 diabetes as cells. At those values, cells are insulin resistant.

For the A1C value, the standard of care has risk “steps” for pre-diabetes and diabetes. Thus it reflects a continuum of sorts. However, no or little action is taken for any value below an actual disease diagnosis, that is, an A1C value above 6.4 percent. When a doctor reviews labs, you are never told about shades of grey. Instead, you are told either a biomarker is “ok” or “abnormal.” This is a naive view of health and unacceptable for people striving to maintain or achieve good health. Ignoring the fact that health and disease are a continuum explains why sixty percent of Americans have at least one chronic condition.

The A1C value is a familiar blood marker value, and many of us know that we do not want to be pre-diabetic (A1C 5.7 - 6.4%). However, many other markers are far more impactful at indicating your current (acute) and future (chronic) state of health. To be healthy, people need to know a good “pre-disease” level instead of the level that classifies us on the wrong side of the health/sick point. For example, a good friend had an A1C of 6.4 percent and was told by her doctor, “all your labs are fine.” This conclusion is unacceptable because a tiny 0.1% increase in A1C would classify her as diabetic. And at that level, she would have been put on a drug while not advised on how to lower that value.

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This is sick care, not healthcare.

Confidence in reference range values is not instilled upon deciphering the definitions applied to them. However, these ranges are standard throughout the world.

Here is an excerpt from testing.com:⁹⁶

“Some lab tests provide a simple "yes" or "no" answer. For instance, was the test positive for the bacteria that cause strep throat? Many other tests, however, are reported as numbers or values. Laboratory test results reported as numbers are not meaningful by themselves. Instead, their meaning comes from comparison to reference values. Reference values are the values expected of a healthy person. They are sometimes called "normal" values.”

The statement, "these values are expected of a healthy person," is false. Reference values are based on the population who obtain labs during a doctor visit. People who visit their doctor are less healthy than those who do not. These reference ranges are adjusted as people descend into poor health over time. Figure 4.3 provides an example how references ranges have changed for WBC counts using population data, not science.

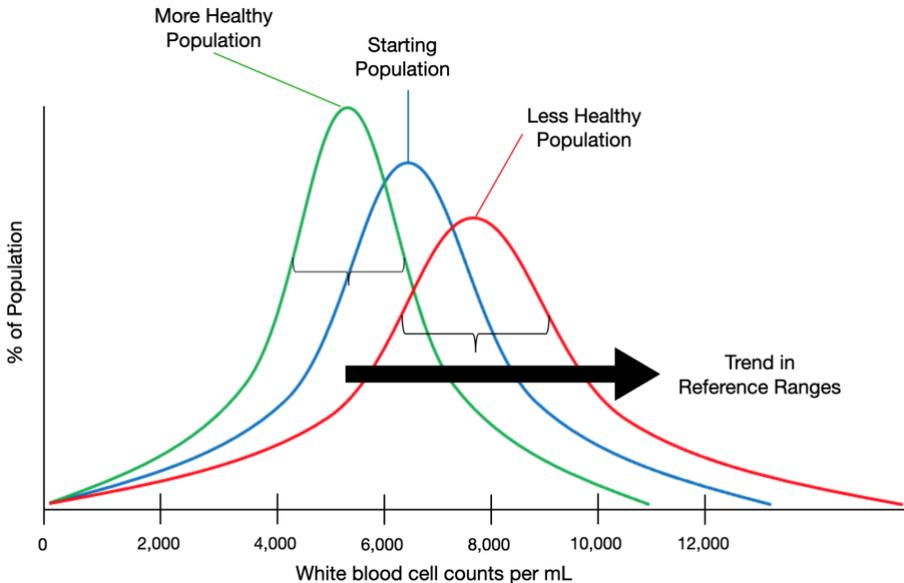


Figure 4.3. Broadening of reference range as the population becomes less healthy (blue to red curves) and narrowing of the reference range as the population becomes healthier (blue to green curves) using WBC counts as an example. The

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transition from the starting population to the less healthy population is a manifestation of reference ranges that do not measure health accurately.

Reference ranges are values derived by evaluating unhealthy people!

There are important facts you need to know about reference ranges:

1. "A normal result in one lab may be abnormal in another: You must use the range supplied by the laboratory that performed your test to evaluate whether your results are "within normal limits." While the accuracy of laboratory testing has significantly evolved over the past few decades, some lab-to-lab variability can occur due to differences in testing equipment, chemical reagents used, and analysis techniques. Consequently, most lab tests have no universally applicable reference value."

Note the way the statement about reference range variability makes it sound almost scientific. Reference ranges do not change frequently. When they do, it is usually by consensus of large medical societies and other interests. For example, the range for total cholesterol continues to tighten in favor of the prescription of statin and other lipid-lowering drugs.

The range of normal white blood cell count has widened. This broader range protects doctors from liability if patients do poorly or die without treatment. When the lab value is "normal," and the patient dies, the doctor does NOT incur liability. Thus, wider ranges protect doctors. There is no clear one-for-one drug to lower white blood cell counts, so the reference range on the high side is close to that measured in people with sepsis. You must be far down the wrong side of the health-disease continuum to have a white blood cell count outside the normal reference range. Essentially you are already sick.

2. "A normal result does not promise health: While having all test results within normal limits is certainly a good sign, it's not a guarantee. For many tests, there is a lot of overlap among results from healthy people and those with diseases, so there is still a chance that there could be an undetected problem. Lab test results in some people with disease fall within the reference range, especially in the early stages of a disease."

Do you find the statement, "there is a lot of overlap among results from healthy people and those with diseases," shocking? Isn't medicine sufficiently advanced to have ranges that define the difference between healthy people and those with a disease? By definition, current reference ranges are useless.

The Women's Health Initiative, a very large prospective study, shows that women with a white blood cell count of 6700 have twice the fatal heart disease compared to women with a white blood cell count of 4700. The upper value of normal for the reference range is ~11,000. So clearly, in the case of women having a white blood cell count over 6700 but below 11,000, the reference range is scientifically

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proven not to be promised good health. Do you want to be told your lab value for white blood cells is normal even though your risk of dying young is significantly elevated?

3. "An abnormal result does not mean you are sick: A test result outside the reference range may or may not indicate a problem. Since many reference values are based on statistical ranges in healthy (not true) people, you may be one of the healthy people outside the statistical range, especially if your value is close to the expected reference range. However, the abnormal value does alert your healthcare provider to a possible problem, especially if your test result is far outside the expected values."

Your cholesterol value is an interesting example of a lab that, when not within the reference range but instead is above "normal" indicates you are healthy.

The reference range for cholesterol is completely wrong.

When people score above the reference range for cholesterol, these healthy people are put on a statin or other cholesterol-lowering drugs. Why? Statins are the most profitable of all drugs. The dark side of statins is that they cause various diseases a person would not get if not on the drug. Congestive heart failure is one such disease. The treatments for congestive are very expensive, harmful, and sometimes invasive. Statins are "off patent" and, therefore, not expensive. However, the downstream costs associated with statin prescriptions are very pricey.

Statin drugs are the gift that keeps on giving money to drug companies.

The explanation of reference ranges is further exemplary as to why the standard of care must be dismantled. The CDC states that 90% of illness and healthcare dollars are for chronic conditions. A chronic disease, by definition, does not kill quickly. Therefore, it can "smolder" for a long time before accelerating into a bad result. Lab values for people with even severe chronic conditions often do not rise too high or become too low. They remain in "smoldering" levels – and rarely leave the broad confines of reference ranges. Doctors are protected from liability!

As chronic condition progress, symptoms and lab values follow the bell curve, with biomarkers rising rapidly and sometimes surpassing the reference range's upper or lower limit. Regrettably, these measurements are often obtained too late, usually after a tragic health event. What percentage of people who have a heart attack know it is coming? Arguably none of them.

Summary:

- A normal result varies from lab-to-lab - for the same test!
- A normal result does not promise health, and
- An abnormal result does not mean you are sick.

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Do you find the way the standard of care makes conclusions about your health disturbing? Can science be applied to improve the accuracy of reference ranges? Humans landed on the moon in 1969. We can do better today. The relationship between biomarkers and early mortality risk data is well-studied and published. Using early mortality to define reference ranges is a science-based approach to defining real normal values.

It is time to roll up our intellectual sleeves and dig deep into what real health looks like, specifically, how to measure it, and move to the healthier side of the health-disease continuum. It is all about determining root causes. Risks leading to early death are paramount to uncover and understand. Redefining what a single biomarker conveys about health is the right starting point. However, defining and using a properly defined reference range for a single biomarker does not overcome the diagnostic deficiencies of current medicine.

Using early mortality as a reference point is the right endpoint. There are many “morbidity,” but death is a singular endpoint for all of us. The risk of dying young is the ultimate measurement of health. Therefore, knowing when biomarkers predict early death or indicate no such risk is a scientific way to establish meaningful reference ranges.

This section presents a detailed scientific exercise on determining the right reference ranges for two biomarkers, WBCs and the red blood cell distribution width measurement (RDW). WBCs reflect the activity of your innate immune system. RDW is more complicated because it is less specific compared to WBCs. Highly elevated RDW values are classically associated with anemia. However, upon more careful review of the science behind the “life and times” of red blood cells, four ranges emerge; a low, an optimal, an inflammation, and an anemia range.

For the RDW biomarker, the inflammation range is not considered in the standard of care. Current reference ranges for RDW consider the inflammation range “normal.” Most chronic diseases involve inflammation, so your traditional doctor is not getting information about the most significant driver of disease when they use the current reference ranges for the RDW biomarker. When comparing science-based reference ranges to the subjective ones used to evaluate your health, it becomes immediately apparent why there is so much sickness, disease, and costs associated with our failed sick care model.

White Blood Cell Count (WBC)

Determining the right reference range is laborious and involves searching deep into the medical literature published in the National Library of Medicine and beyond. It starts with a basic search of the terms “WBC” and “mortality.” This search yields 260,000 references. The combination term “white blood cell” and mortality yields an equally daunting number of references, specifically 305,000. Fortunately, search engines provide refinements, one of which is “word in the title

of the document only.” Using this search strategy yields 17 and 149 references, respectively. The term “survival” is another way mortality data is expressed. The title-only search with survival substituted for mortality yields 25 and 52 references, respectively. These 200 or so references are the starting point for researching and ascertaining the relationship between WBC and mortality on the way to establishing a scientific reference range.

Indeed, mortality is not a perfect endpoint for biomarker reference ranges. Therefore, view the reference range derived from early mortality data as scientific but still not completely optimal. For example, based on early mortality data, the proper reference range for WBCs is 4,000 – 5,700 counts/mL. The healthiest people have WBC counts of 4,200 – 4,600. This optimal range is based on subjective clinical experience and not upon the objective mortality endpoint. Optimal values are never reported in the medical literature. However, since our team measures and scores risks with great precision, the "optimal" scale we define is driven by clinical data. Figure 4.4 shows the optimal and "no excess early mortality risk" levels for the WBC biomarker.

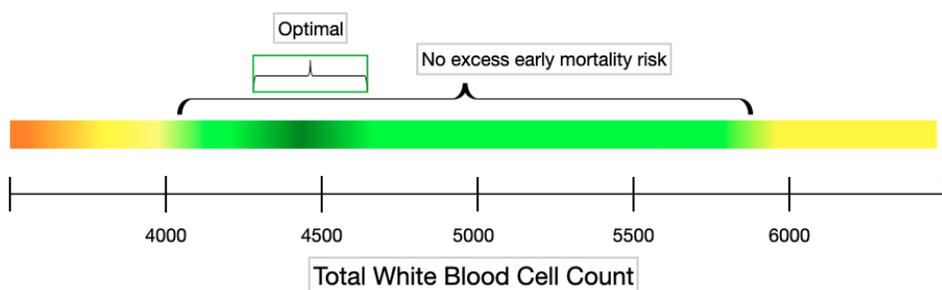


Figure 4.4. The science-based reference range for total white blood cell count. Orange range, moderately elevated mortality risk; yellow range, slightly elevated mortality risk range; light green, no increase in mortality risk range; and dark green, optimal health range.

The next task is to read the papers that link WBC and mortality to evaluate the statistics behind the studies. Many papers are eliminated because not all the studies with the right title have the right data. In medical speak, the study performed was not properly “powered” to draw definitive conclusions about the relationship between the variables, the biomarker value, and early mortality risk. However, plenty of studies do meet the “power” criteria for WBC and early “all-cause” mortality risk, so science-based normal ranges can be determined.

The current “normal” ranges for WBC levels are presented in Table 4.2. Compare these values to those presented in Figure 4.4. There are substantial differences.

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Source	WBC (cells/microliter) Normal Range
LabCorp	Varies: 3,400 – 10,800 or 4,500 – 10,000
Mayo Clinic (December 2020)	3,400 – 9,600
Mayo Clinic 2 (Date not given)	4,000 - 11,000
WebMD	4,500 – 11,000
Quest Diagnostics	3,800 – 10,800
MedlinePlus	4,500 – 11,000
Accu Reference Medical Labs*	4,200 – 11,800
Cleveland Clinic	5,000 – 10,000
MedPage Today	5,000 – 12,000

Table 4.2. Standard-of-Care reference ranges for “normal” white blood cell counts are based on the accepted definition of normal levels but not on safe or optimal levels.

LabCorp and Quest Diagnostics are the major testing labs in the United States. Your doctor then explains that you are normal and healthy if your WBC count is below 10,800, or 9,600, or 10,000, or 12,000, or 11,000 on the high end of the normal range. Your doctor may also declare you are in good health if your WBC count is above 3,400, or 3,800, or 4,000, or 4,200, or 4,500, or 5,000. With this kind of variability, your health may be subject to an identity crisis requiring a mood-altering drug.

Variations in reference ranges prove they are baseless and, in fact, harmful. If reference ranges promote health by informing doctors of risks and diseases, population health will improve, assuming doctors and patients implement appropriate protocols to return the values to normal. On the other hand, if the reference ranges do not promote health, the population’s health will worsen. Simple statistical math helps us understand this point. Here are the two scenarios:

Scenario 1. Reference ranges are inaccurate and therefore do not contribute to understanding health. For example, a person who is unhealthy, but considered healthy due to the labs, continues to degenerate. This person’s labs progressively get worse and are reflected in his or her labs. This person’s labs are now included in determining the standard of care population-driven reference ranges. Therefore, the normal ranges change for the worse. Using data on unhealthy people is a key reason why reference ranges are inaccurate.

Scenario 2. Reference ranges are accurate and thus contribute to a proper medical workup and related interventions. In this instance, people are directed towards better health. In this scenario, the general population becomes healthier, and chronic diseases diminish rather than proliferate.

See figure 4.3 above as it illustrates the processes described in the two scenarios.

The wide ranges assumed to reflect normal values are certainly not consistent with humans being genetically 99.9% the same. The elevation or suppression in counts

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for white blood cells is due to an infectious disease process. Is it not obvious that healthy humans would, in general, have very similar WBC counts? Glucose standard levels are more reasonable. The upper and lower limits to the reference range are 70 – 99 mg/dL, a 29% variation. However, the WBC count variation is 263% variation. Blood sugar changes rapidly with food intake. WBC counts are much more stable in comparison. That the WBC normal range is substantially broader compared to glucose is a good indicator that the range is wrong.

Sepsis is defined as a life-threatening infection. According to the CDC, “Sepsis is the body’s extreme response to an infection. Therefore, it is a life-threatening medical emergency. Sepsis happens when an infection you already have triggered a chain reaction throughout your body. Infections that lead to sepsis often start in the lung, urinary tract, skin, or gastrointestinal tract. Without timely treatment, sepsis can rapidly lead to tissue damage, organ failure, and death.”⁹⁷

Leukopenia is defined as low levels of WBCs, while leukocytosis refers to high WBCs. In most cases of sepsis, leukocytosis is the case. However, WBC counts are not always above the reference range, yet many people still have a diagnosis of sepsis. In fact, they do have sepsis – a life-threatening acute infectious condition. How can this be? How can a person have a diagnosis of sepsis while having a so-called normal level for their WBC?

One source discussing sepsis and WBC counts is the EMCrit Project,⁹⁸ which states:

“Sepsis can cause the WBC to increase or decrease!”

EMCrit goes on to say, "WBC is fundamentally a garbage parameter, used predominantly due to convenience and tradition."

"Very rarely, the WBC is actually helpful:

- True neutropenia is a big deal (e.g., patients may require broad-spectrum antibiotic coverage for neutropenic fever).
- If the WBC is crazy high, something bad is probably going on. However, in this situation, the neutrophil/lymphocyte ratio will also be haywire, so the WBC count probably doesn't add much information beyond the neutrophil/lymphocyte ratio.
- Again, for the folks in the back: A normal WBC says nothing about septic shock. Lots of patients with septic shock will have a stone-cold normal WBC."

Here is a translation of what the EMcrit site states:

Your innate immune response (WBCs) cannot measure your innate immune response!

This summary by EMCrit is garbage. Accurately measuring WBC counts is not.

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Is the reference ranges they use to draw their conclusions not accurate? Interesting. EMCrit is devoted, according to their website, to "Maximally Aggressive Care: Maximally Aggressive Curative Care and Maximally Aggressive Palliative Care." God help their pre-sepsis patients.

Another source of information on sepsis and WBC counts is a group from South Korea. They published a paper titled "Identification of the robust predictor for sepsis based on clustering analysis."⁹⁹ Some excerpts from this paper include:

"The WBC levels in elderly subjects exhibited insignificant association with the sepsis status. Aminzadeh et al. reported that only 60% and 6% of sepsis subjects had $WBC \geq 14,000$ and $< 4,000$ WBC counts, respectively. In a study by Caterino et al.,¹⁰⁰ WBC's predictive performance was poor for classifying sepsis. In elderly patients, as aging progresses, chronic inflammatory status is pervasive, and cell regeneration ability and phagocytosis are reduced. For these reasons, the response of neutrophils to infection can be delayed. Therefore, the normal neutrophil count should not be allowed to exclude patients from being diagnosed with sepsis in an elderly population."

"Laboratory markers used for the diagnosis of sepsis have low screening power in a specific population group. For example, Seigel et al. pinpointed that about 52% of patients with bacteremia had a normal range of WBC levels, and 21% of patients diagnosed with severe sepsis or septic shock manifested a normal WBC count at the time of admission to the emergency department. Consequently, there have been tremendous efforts to find the sensitive and suitable marker that would be used for early diagnosis of sepsis."

Neither of these sources considered that the diagnostic problem concerning WBC counts is the normal range – not the marker itself. There is no need to scuttle the WBC count. Adding more biomarkers is always valuable in providing a complete health story. The words of Jack C. de la Torre, M.D., senior editor for the Journal of Alzheimer's Disease, add clarity to the WBC conundrum indicated by the Koreans and EMCrit, from his paper titled, "A Tipping Point for Alzheimer's Disease Research."¹⁰¹

"A drunkard loses his keys on a dark street and is looking for them under a lamppost. A policeman comes over and asks what he's doing. 'I'm looking for my keys,' he says. 'I lost them over there.' The policeman looks puzzled. 'Then why are you looking for them over here?' 'Because,' replies the drunk, 'the light is much better here. There is an undeniable logic to looking for things lost in the dark where the light is better. But when the search under the light consistently yields nothing, it is wiser to move on and look elsewhere, even where the light is dim.'"

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The “keys” in the de la Torre soliloquy are your white blood cells. Regrettably, medicine is looking in the wrong place on the WBC count continuum. When interpreted correctly, using a science-based reference range, WBCs are extraordinarily powerful at measuring and predicting chronic diseases and infections like sepsis. However, it is hard to state how inaccurate the WBC reference ranges are when sepsis, a severe acute infectious process, cannot even be diagnosed with the current ranges.

The reference range for WBCs must change dramatically.

Renown studies refute the conclusions about the lack of predictive value of WBC counts. And in so doing, they further illustrate the inexactitude of the established reference ranges. For example, a key study is the Women’s Health Initiative (WHI). This study is valuable because of the ~66,000 people (cohort) in the study.

By way of The Harvard Gazette,¹ Harvard University capsulizes the WHI data and comes close to identifying a proper upper WBC value, at least on the high side. Their March 17, 2005 article titled “Simple test predicts heart attack. White blood cells sound a new alarm.”¹⁰² Excerpts are included here.

“White blood cell levels are a good predictor of strokes, heart attacks, and fatal heart disease in older women, according to a nationwide study. In addition, white cell counts can be easily measured by inexpensive, widely available tests, raising the possibility of lowering the toll of heart disease fatalities, the leading cause of death among women in the United States.”

"For years, researchers have suspected a link between elevated white blood cell count and heart attack," notes Dr. JoAnn Manson, one of the study leaders and Elizabeth F. Brigham Professor of Women's Health at Harvard Medical School. "The present study is the largest to test this association and provides the strongest evidence to date that WBC [white blood cell] count predicts the risk of a heart attack."

“As part of the federally supported Women's Health Initiative, investigators at medical centers all over the United States collected information on 72,242 postmenopausal women 50 to 79 years old. All were free of heart and blood vessel disease at the start of the study. During six years of follow-up, 1,626 heart disease deaths, heart attacks, and strokes occurred. Women with more than 6.7 billion white cells per liter of blood (6,700 WBC/ml) had more than double the risk of fatal heart disease than women with 4.7 billion cells per liter or lower (4,700). A count of 6.7 is

¹ The Harvard Gazette is the official news website of Harvard University, and highlights innovation and discovery in teaching, learning, and research.

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considered normal, so what is "normal" may have to be redefined." Figure 4.5.

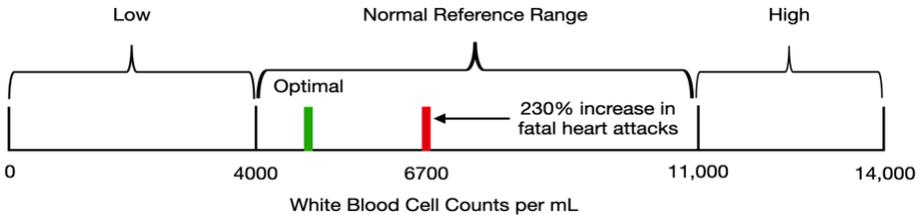


Figure 4.5. WBC count low, normal, and high ranges based on the current standard of care values. In women, fatal heart attacks increase by 230% at a "normal value."

"Women with the highest counts (6,700, compared to the standard-of-care upper limited of 10,800) had a 40 percent higher risk of nonfatal heart attack, 46 percent higher risk of stroke, and a 50 percent greater risk of death from all causes."

"Manson (the study author) also believes that white blood cell counts apply to younger as well as older women."

Note that this article was published in 2005. Since then, the "upper limit" for WBC good health your doctor uses has gone UP, not DONE. And heart-related diseases continue to be our number one killer. Figure 4.5 provides a shocking yet self-evident explanation for this statistic.

The original research is presented in an article titled "Leukocyte count in vascular risk prediction."¹⁰³ A leukocyte is another term for a white blood cell. This editorial article is based on the fine work of Margolis and colleagues from Harvard Medical School and seven other major health centers.¹⁰⁴ Here is a summary of the article.

"The major finding of the study was that leukocyte (WBC) count in the top quarter of the population distribution ($>6.71 \times 10^9$ cells/L) was associated with an approximate 50% increase in the risk of myocardial infarction (heart attack), stroke, total vascular disease, and total mortality, independent of other risk factors. The risk of coronary death was higher, estimated as a 230% increase."

"The association was similar even among women who did not self-report the presence of major cardiovascular risk factors. Findings are consistent with other studies of leukocyte (WBC) count and vascular events."¹⁰⁵

What is most interesting about this result is that known risk factors did not impact the predictive power of WBC. Therefore, if you "watch your numbers" like we are told, which usually means your total cholesterol numbers, it has no impact on your health if you do not manage your elevated WBC count.

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Be forewarned that doctors practicing the standard of care will disregard this information or suggest that there are insufficient studies to support the finding. But the statistics on this study show the data is definitive:

“Margolis and colleagues from the Women’s Health Initiative (WHI) Research Group report that a higher leukocyte (WBC) count is associated with an increased risk of cardiovascular events and mortality among 66,261 women at 40 (medical) centers followed in the WHI Observational Study.”

The value >6,700 is based on the evaluation of over 66,000 women. It is a study with a massive amount of data. Studies involving 1000 or more are considered quite large. The gold standard randomized, double-blinded, placebo-controlled trials used to approve new drugs evaluate between several hundred to about 3,000 people. The WHI study that shows the predictive value of WBC counts included 4,000 percent more participants. There is no disputing the data from a study of this magnitude.

The WHI is not the only study that provides objective data on what should be the normal reference range for WBC counts. America's own National Institute on Aging and National Institutes of Health weighed in on white blood cell counts. A team from the NIH and Italy produced a study titled “White Blood Cell Count and Mortality in the Baltimore Longitudinal Study of Aging.”¹⁰⁶ They start their paper with a strong statement about the value of WBC counts.

“White blood cell (WBC) count is a marker of systemic inflammation, and elevated WBC count is associated with all-cause mortality¹⁰⁷ as well as cancer,¹⁰⁸ cerebrovascular,¹⁰⁹ and cardiovascular¹¹⁰ mortality. The WBC count is an independent risk factor for cardiovascular and cerebrovascular events.”¹¹¹

That is a strong endorsement for this readily available and inexpensive biomarker of the innate immune response. The National Institutes of Health concluded:

“Participants with baseline WBC <3,500 cells/mm³ and WBC >6,000 cells/mm³ had higher mortality than those with 3,500 to 6,000 WBC/mm³.”

“Participants who died had higher WBC than those who survived, and the difference was statistically significant within five years before death.”

This very important study teaches us a few things.

- First, WBC < 3,500 is a prognosticator of early and unnecessary mortality. Lower white blood cell counts are often associated with pathogenic viral infections and associated cancers.
- Second, several of the reported reference ranges indicate WBC counts are abnormal in a range that is actually normal, specifically between approximately 4,000 and 5,000 cells/mL.

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- With regard to white blood cell counts, modern medicine uses the wrong reference range on the high and low end.
- Third, $WBC > 6,000$ cells/mL is a prognosticator of early and unnecessary mortality. The WBC is elevated (at least) 5 years before death; thus, it is a strong diagnostic predictor of your future longevity. A comparison between the data from this NIH paper, published in 2007, and so-called authoritative sources that determine reference ranges is shown in Table 4.3.

Source	WBC Lower Normal	WBC Upper Normal
2007 Study	3,500	5,700
Standard Reference Range	4,200	10,900

Table 4.3. WBC ranges. Row 1 shows ranges based on the risk of dying young from a 2007 study. Row 2 shows the average standard of care reference ranges.

Everyone who relies on their doctors, the major clinical laboratories, and the authoritative medical establishment, who have a $WBC > 5,700$ but less than 10,900, are at much greater risk of dying or suffering from severe cardiovascular disease. What percentage of the U.S. population is between 5,700 and 10,900? Guess a lot! How can we be so sure? Death from cardiovascular diseases is the #1 killer of Americans, and in the case of famous people like Tim Russett and Bernard Tyson, medicine claims to be baffled.

Two studies provide bookends to the timeline for understanding normal versus abnormal WBC counts. The purpose is to show that this information is not new and continues to be investigated, but the research is not influencing those who dictate the standard of care clinical delivery.

Study 1. October 11, 1985. “Prognostic Importance of the White Blood Cell Count for Coronary, Cancer, and All-Cause Mortality.”¹¹² The key points made in this article include the following.

- For each decrease in WBC count of 1,000 per mL, the risk for coronary heart disease death decreased by 14% (when higher than 6,000 counts per mL)
- On average, people with a WBC count of 7,750 per mL had worse outcomes than those with average counts of 6,080 per mL.

The article abstract is reproduced here.

“The relationship of white blood cell count (WBC) to fatal and nonfatal coronary heart disease (CHD) incidence and all-cause and cancer mortality was assessed in a subset of participants in the Multiple Risk Factor Intervention Trial (MRFIT). For this group of 6,222 middle-aged men, the total WBC count is strongly and significantly related to the risk of CHD,

independent of smoking status. In addition, change in WBC count from baseline to the annual examination just before the CHD event was found to be a significant and independent predictor of CHD risk.

For each decrease in WBC count of 1,000 cu mm, the risk for CHD death decreased by 14%, controlling for baseline WBC count and other CHD risk factors (smoking, cholesterol level, diastolic blood pressure). In addition, the WBC count was strongly related cross-sectionally to cigarette smoking and smoking status, as indicated by serum thiocyanate concentration. Smokers, on average, had a WBC count of 7,750/cu mm compared with 6,080/cu mm for nonsmokers. The WBC count was also significantly associated with cancer death, independent of reported smoking and serum thiocyanate levels."

Study 2. November 18, 2021. "Is White Blood Cell Count Associated with Mortality in Peritoneal Dialysis Patients? A Retrospective Single-Center Analysis." This paper is important because the authors show all-cause mortality in "tertiles" – three different ranges of WBC counts. They also performed mathematical modeling to create a continuous scale of all-cause mortality. They understand that health and disease are a continuum! Several illuminating conclusions emerge from this study.

- When the WBC count was modeled as a continuous variable, survival models were created. The finding was mortality risk increased by 23 percent for every 1000 WBC count per mL increase (on the high side of normal WBC counts).
- All-cause mortality increased by 270 percent when WBC increased from <8,200 counts/mL to 8,200 - 10,500 counts/mL. This second range is considered normal by doctors throughout the world.
- WBC counts above 10,500 per mL led to a 450% in all-cause mortality compared to the <8,200 per mL group. A WBC count above 10,500 is considered normal by some labs and authorities that provide reference values.
- Total cholesterol levels were essentially the same across all groups. Therefore, cholesterol provided no diagnostic value for all-cause mortality.

A 2022 paper concluded that people who suffer a heart attack and have to be hospitalized die in proportion to their WBC counts. This paper does not give WBC count ranges, however. It is titled "Correlation between White Blood Cell Count and Myocardial Infarction Mortality in Patients admitted at Tertiary Care Center of Philippines."¹¹³

Figure 4.6 shows the relationship between WBC counts and all-cause mortality in the continuously variable model.

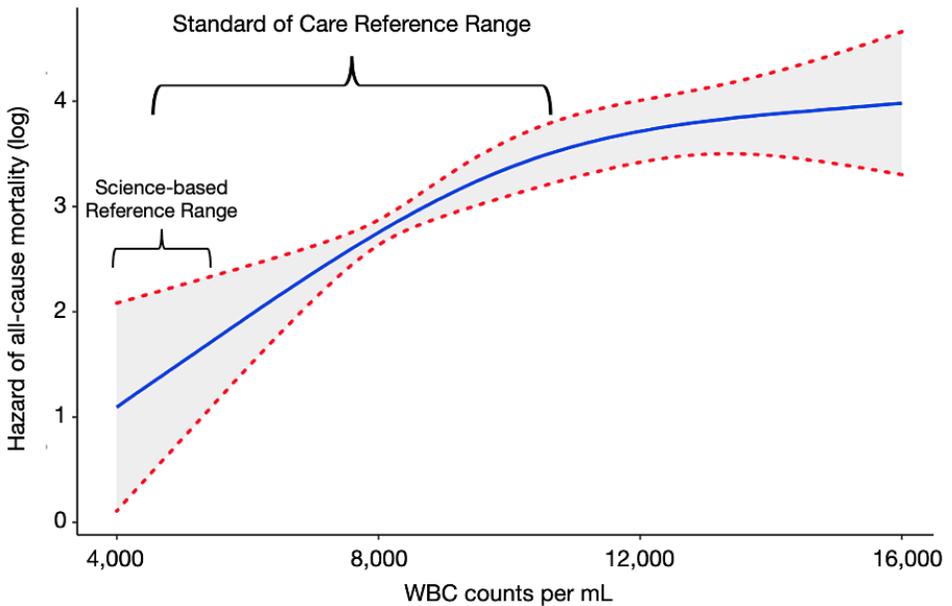


Figure 4.6. The association between log-relative hazard of all-cause mortality and the white blood cell count.

This research study did not evaluate low levels of white blood cell counts. Based on a substantial number of related research studies, the hazard of dying young increases much more dramatically below 4,000 counts per mL than levels above 5,700 counts. The proper range for WBC counts for optimal health is 4,000 – 5,700, based on mortality data. The data on the lower end of the spectrum is less studied as most research lumps low values into a group that overlaps with the true normal range making it difficult to accurately evaluate this region.

Another large, well-respected study is the National Health and Nutrition Examination Survey (NHANES I, II, and III). An abstract from one of the many publications produced by this study provides an excellent summary.

“Inflammation is a risk factor for several chronic diseases. However, few epidemiologic studies have examined the relationship between markers of inflammation and cancer. The current study included 7,674 Second National Health and Nutrition Examination Survey (NHANES II) participants, 30 to 74 years of age, between 1976 and 1980. Mortality follow-up through December 31, 1992, was assessed using the National Death Index and Social Security Administration Death Master File.

A graded association between higher WBC and higher risk of total cancer mortality was observed [highest versus lowest quartile (relative risk [RR] 2.23; 95% confidence interval [CI], 1.53-3.23)] after adjusting for age, sex, and race. After further adjustment for smoking, physical activity, body mass index, alcohol intake, education, hematocrit, and diabetes, WBC

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remained significantly associated (P trend = 0.03) with total cancer mortality [highest versus lowest quartile (RR 1.66; 95% CI, 1.08-2.56)].

These findings support the hypothesis that inflammation is an independent risk factor for cancer mortality. Additional studies are needed to determine whether circulating inflammatory markers are associated with increased risk of incident cancer.”

Realize that WBC counts do not measure inflammation directly. Instead, they are a measure of infectious burden. Inflammation is the immune response to the infection. Key summary points from the study are:

- Seven thousand six hundred seventy-four people were included in the study findings, approximately 300% more than in randomized trials used to approve a drug.
- People with optimal WBC counts are over 200% less likely to die from cancer.

The data provides bona fide proof that cancer is an infectious disease in many cases. In these instances, WBC counts are outside the science-based normal range.

Figure 4.7 presents a summary of the NHANES II data.

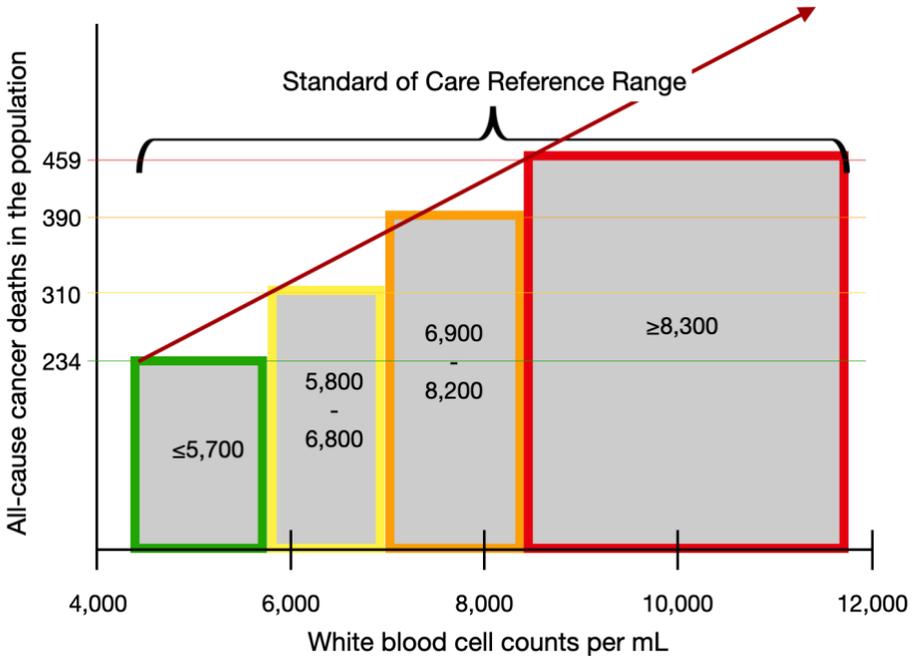


Figure 4.7. Risk of cancer all-cause mortality by quartile (groups) of WBC counts from the NHANES II study.

Federal health officials are fully aware that the standard of care reference ranges is incorrect. A study from the Centers for Disease Control and Prevention (CDC)

evaluated 8,355 participants from 1999-2002 for emerging risk factors that could contribute to higher cardiovascular disease risk. The study's results showed that an elevated WBC count ($>7,000$) was associated with a 49% increase in the likelihood of a person being in the highest coronary heart disease risk category. The research supporting this data is presented in a publication titled "Distribution of lifestyle and emerging risk factors by 10-year risk for coronary heart disease."

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Elevated WBC count in the elderly predicts survival. A Swedish group presented their data in a research article titled "White Blood Cell Count in Elderly Is Clinically Useful in Predicting Long-Term Survival."¹¹⁵ More than 425 swedes 75 years old participated in the study. The average WBC count for men and women in the study was 6,300 and 5,700, respectively. There was a 16% increase in mortality for men and a 28% increase for women for every 1,000 increases in WBC counts. The authors conclude, "The WBC count deserves attention as a potentially clinically useful predictor of survival in the 75-year-olds, especially among women."

This study infers that the upper limit of a true normal WBC count, at least for women, is 5,700 per mL. The WBC count of 5,700 is the lowest scientifically valid upper limit for normal published as of 2022.

Low WBC counts, more medically known as leukopenia, are not well studied. An example publication discussing leukopenia and mortality is titled "Leukopenia (WBC <4) Rather than Leukocytosis (WBC >14) Within 48 Hours of Admission Has a Greater Impact on Mortality Following Trauma; An Analysis of 2,467 Patients." "The authors' state:

"Considerable volumes of data have focused on the significance of an elevated WBC as a marker of the degree of Systemic Inflammatory Response Syndrome and inflammation. However, almost no data addresses the impact of leukopenia. This is when WBC counts are below 4,000 compared to patients who mount a leukocytosis (high WBC counts) response."

This study established the following.

"We clearly demonstrate that there is a greater impact on outcomes such as hospital and ICU length of stay, and ultimately mortality, especially in the young, from leukopenia (WBC $<4,000$ /mL rather than leukocytosis ($>12,000$ /mL) following hospitalization for traumatic injuries."

This study, conducted by the NIH, demonstrated that "Participants with baseline WBC $<3,500$ cells/mm³ and WBC $>6,000$ cells/mm³ had higher mortality than those with 3,500 to 6,000 WBC counts/mm³."

The National Registry of Myocardial Infarction (NRMI – an MI is also known as a heart attack) is one of the oldest and largest registries of acute myocardial

infarction (AMI). The word “acute” describes a heart attack, but the actual event is the only thing sudden about a heart attack. Heart attacks are actually chronic events with a decades-long incubation period. The NRMH launched four studies starting in 1990. In all, 1600 hospitals participated, and >2.2 million patients were followed. This volume of information removes all doubt about the statistical strength of the findings, Figure 4.8.

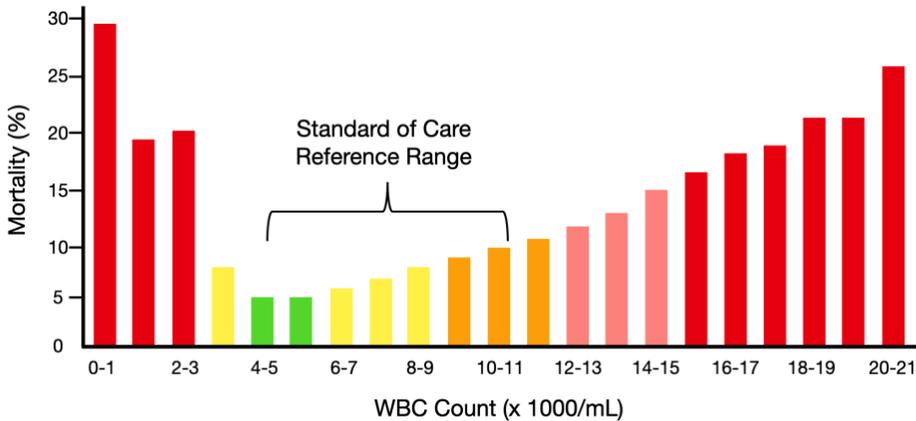


Figure 4.8. In-hospital mortality by white blood cell counts. The information was obtained over 30 years with greater than 2.2 million patients.

The researchers conclude, “The white blood cell count is an independent predictor of in-hospital mortality and may be useful in assessing the prognosis of AMI (heart attack). The precise clinical-pathophysiologic link between the WBC count, the underlying inflammatory process, and clinical correlates and events associated with AMI remains unclear. We suggest that the WBC count should be considered in the prognostic risk stratification of AMI patients upon presentation.”

The authors of this study need to review basic immunology. White blood cell counts become above or below normal values because of infection. Here is a peek at the professional pedigree of the authors of this impressive study.

Mary Grzybowski, Ph.D., MPH. is Assistant Professor of Epidemiology, Brody School of Medicine, Dept. of Public Health, East Carolina University, Greenville, NC

Hal V. Barron, MD, is an American clinician-scientist and drug developer who has been president of research and development at GlaxoSmithKline since March 2018. Before this, he served as president of research and development at Calico.

Robert D. Welch, MD, is a clinician in emergency medicine, a clinical researcher, a Director of Clinical Research, and a Fellowship Director of Clinical Research at Wayne State school of medicine.

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Chiadi Ndumele, MD, Ph.D., is the Robert E. Meyerhoff Assistant Professor in the Department of Medicine at Johns Hopkins University.

Robert Zalenski, MD, is the Medical Director of Palliative Care at St. Joseph Mercy Oakland. Served as National Medical Director for Vanguard Health and Tenet Health, guiding the development of numerous hospital-based palliative care programs across the United States.

Their study and data analysis were extraordinarily informative. However, data is useless if not properly interpreted and used to implement impactful clinical protocols. I am sure all these professionals do their best for patient care. The conclusion to their paper, however, does not instill confidence.

Early mortality, an endpoint to establish normal ranges, is a “worse case” scientific endpoint. Therefore, the normal range must err on the side of optimal health. Thus, when using the data to determine the lower limit of normal WBC counts, the highest value indicating early mortality risk defines the lower limit of the normal range. Leukopenia, therefore, begins at 4,000 WBC counts per mL based on the available data.

The current normal range for WBC counts is based on early all-cause mortality data. Therefore, these values are subject to change as new information becomes available. The normal ranges are provided in Table 4.4.

Source	WBC Lower Normal	WBC Upper Normal
Normal Based on Mortality Data	4,000 per mL	5,700 per mL
Average Standard Reference Range	4,200 per mL	10,900 per mL

Table 4.4. WBC normal ranges Row 1. The risk of dying young is the basis of the ranges. Row 2. The average standard of care reference ranges derived from several so-called authoritative sources.

If you want to enjoy optimal health, the ideal WBC count is 4,200 – 4,600 WBC counts. This is based on the clinical assessment of very healthy people. So having a WBC count in this range should be the goal of everybody.

Many clinical studies on white blood cell counts are on older people. However, WBC counts are equally meaningful to young people. White blood cells are innate immunity, and babies have them too. Thus, is WBC count important to know for the young, or is it just a consideration for the elderly? A broad group of U.S. researchers answered this question. The paper they compiled is titled “White blood cell count in young adulthood and coronary artery calcification in early middle age: coronary artery risk development in young adults (CARDIA) study.”¹¹⁶ Here are some highlights.

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“White blood cell count is associated with incident coronary heart disease (CHD). However, data are sparse regarding its association in young adults with future coronary artery calcification (CAC).”

The study involved over 3000 young people (18 to 30 years old) and followed them for 15 years, with a follow-up in an additional five years.

Baseline total WBC counts in young adults were associated prospectively (looking into the future) with coronary artery calcification presence 20 years later after adjusting for age, sex, and race. That is, elevated levels of WBC in the young are correlated with disease development in middle age.

“Our results suggest the possible early involvement of WBC, particularly eosinophils,² in the early stages of atherosclerosis.”

WBC count is a predictor of future disease for very young adults. Since chronic diseases have smoldered, potentially for decades, the WBC counts in young people should be in the optimal region of the normal range.

WBC and Atrial Fibrillation

I had atrial fibrillation that may have been caused by Lyme disease. Lab tests did not indicate full-blown Lyme disease, but two “bands” for Lyme were positive. I took two antibiotics for an extended period to overcome the disease. This is one of the very few treatment types for chronic infections.

Acute infections must be treated acutely (short-term). Chronic infections must be treated chronically (long-term).

Today, my heart is in sinus rhythm. I experienced a very strong whole-body Jarisch Herxheimer reaction for the first three days of the treatment, indicating a bacterial “die-off” reaction. This reaction indicates two things.

1. A "die off" reaction of stealth pathogens of some type occurred.
2. The treatment was appropriate for the condition.

“The Jarisch Herxheimer reaction (JHR) is a transient clinical phenomenon in patients infected by spirochetes who undergo antibiotic treatment. The reaction occurs within 24 hours of antibiotic treatment of spirochete infections, including syphilis, leptospirosis, Lyme disease, and relapsing fever.”¹¹⁷ The standard definition is a bit narrow. When almost any organism capable of evading the

² Eosinophils are white blood cells and one of the immune system components responsible for combating multicellular parasites and certain infections. Apparently chronic infections that start in our youth can persist and cause clinical disease 20 years later.

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immune system is properly treated, the immune system will elicit a JHR. When you have the flu and feel lousy, that is the JHR induced by your immune system.

Your immune system is antibiotic.

The Framingham Heart Study is modern history's most respected study on cardiovascular disease. A paper titled "White Blood Cell Count and Risk of Incident Atrial Fibrillation (From the Framingham Heart Study)" contributes to the discourse on the risks of slightly elevated WBC counts.¹¹⁸ According to the author, "Several studies have reported that inflammatory markers are associated with atrial fibrillation (AF). The white blood cell (WBC) count is a widely available and broadly used marker of systemic inflammation. Our sample consisted of 936 participants with an average age of 76. The white blood cell count (WBC) was 5,600 to 7,800. An increased WBC count (within that range of 5,600 to 7,800) was significantly associated with incident AF."

"In conclusion, in our community-based sample, an increased WBC count was associated with incident AF (atrial fibrillation) during five years of follow-up. Our findings provide additional evidence for the relationship between systemic inflammation and AF."

There is that concept of "inflammation" again. Almost 100 papers in the NLM correlate infection with AF. It is time for the medical community to replace the term "inflammation" with infection. Infection is the cause of "inflammatory" diseases, and inflammation is the physiological manifestation. Medical language must switch from "symptoms-speak" to "cause-speak."

Note that the level of WBC counts that induce AF is considered normal in the standard of care. Also, note that the trend in AF as the WBC value increases from 5,600 is consistent with our published normal range for WBC counts of 4,000 - 5,700.

WBC and Cancer

A Japanese team examined the association between white blood cell (WBC) count and the development of gastric cancer by following 2,558 people over the age of 40 for 19 years.¹¹⁹ The people were grouped according to WBC status as follows:

< 4,500; 4,500 – 5,200; 5,300 – 6,300; > 6,300

Age-adjusted and sex-adjusted incidences of gastric cancer increased linearly with higher WBC levels. For example, the risk of gastric cancer is 2.22-fold higher in the highest WBC count group (>6,300) compared to the lowest group. Further, the risk for gastric cancer was even higher in the upper WBC group when the patients tested positive for H. pylori infection.¹²⁰

WBC and COVID-19

The SARS-CoV-2 virus causes changes to WBC counts. Baseline WBC and neutrophil counts generally increased in patients admitted to a hospital or who die

of COVID-19. All COVID-19 groups presented lower baseline counts of lymphocytes and eosinophils than the control group, but these counts were even lower in severe and fatal COVID-19 groups.¹²¹ The elevation of neutrophils (Neutrophilia) and suppression of lymphocytes (Lymphopenia) is best measured with the neutrophil-to-lymphocyte ratio (NLR). The medical research industry is aware of this biomarker as the NLM database contains 72 peer-reviewed publications using a “title-only” search. The importance of the NLR ratio is examined in the next chapter.

In COVID-19, increased neutrophil counts are observed in the blood early into the disease, particularly in severely affected individuals. This is considered a major clinical feature of this synthetic disease when compared and contrasted to other virus-based diseases.¹²² Historically, many studies investigating circulating immune cells in disease have focused on analyzing peripheral blood mononuclear cells, excluding neutrophils. Thus, there is a lack of knowledge about the behavior of this most abundant immune cell fraction in the blood in viral diseases.¹²³

Neutrophils do not always elevate in a viral infection. Interestingly, neutrophils go to lower-than-normal levels in those with the SARS-CoV-2 virus and Epstein Barr. A publication titled “Role of neutrophils in acute viral infection” explains the variation of neutrophils.¹²⁴ This type of deep understanding of the behavior of immune cells emphasizes the need to include as many biomarkers as possible in the patient workup. A quote from the publication is presented here.

“Complex interactions among proliferation, apoptosis, and differentiation processes regulate the number of neutrophils. Since neutrophils are the first line of defense against a viral invasion, the number of neutrophils in the local microenvironment increases sharply following a viral infection. Notably, the number of neutrophils in the respiratory tract is positively correlated with the virulence and dose of the influenza virus. Conversely, in certain viral infections, such as severe fever with thrombocytopenia syndrome virus (SFTSV), the number of neutrophils in circulation is decreased for some reason. For example, when neutrophils migrate to the infected tissues and undergo netosis or apoptosis, the development, differentiation, maturation, and bone marrow mobilization of neutrophils might be affected by viruses, which might negatively affect the neutrophil homeostasis”.

Basic immunity tells us that neutrophils elevate mainly due to bacterial infection. Indeed, early into COVID-19, the Chinese and Harvard Medical School demonstrated that the antibiotic, Azithromycin was an important treatment for the disease. There is little evidence that antibiotics treat viruses, so the assumption is that the SARS-CoV-2 virus facilitates the proliferation of other pathogens that were previously stealth within the COVID-19 sufferer. These “silent” pathogens seek an opportunity to take advantage of vulnerabilities, and the SARS-CoV-2 virus is masterful at creating vulnerabilities.

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Massachusetts General Hospital, a Harvard Medical School teaching hospital, published COVID-19 treatment guidance early into the pandemic. This guidance is most instructive concerning the concept of the health continuum. It also illustrates that top-tier medical research recognized that the novel virus associated with COVID-19 accelerated any existing susceptibility. A section of their guidance is provided in Table 4.5.

Table 1: Work-up for diagnosis, prognosis / risk stratification, and/or safety of therapeutics Suggested for <u>hospitalized</u> patients with confirmed COVID-19¹	
<p><u>Recommended daily labs (until stable):</u></p> <ul style="list-style-type: none"> • CBC with diff (esp. total lymphocyte count) • Complete metabolic panel² • CPK (creatine kinase) • Ferritin/CRP (first 2 wks of hospitalization)³ <p><u>Recommended at baseline then every other day</u> (if in ICU or elevated check daily):</p> <ul style="list-style-type: none"> • PT/PTT/fibrinogen • D-dimer <p>Link to Guidance from MGH Hematology</p>	<p><u>For acute kidney injury</u> (i.e. serum creatinine >0.3 above baseline)</p> <ul style="list-style-type: none"> • Urinalysis and spot urine protein:creatinine <p><u>When MAS/sHLH suspected</u> (rising LFTs, falling fibrinogen, hypotension, see Immunomodulation):</p> <ul style="list-style-type: none"> • ESR <p><u>Viral serologies for all patients unless done recently:</u>⁴</p> <ul style="list-style-type: none"> • HBV serologies (sAb, cAb, and sAg) • HCV antibody, unless positive in past • HIV 1/2 Ab/Ag
<p><u>For risk stratification:</u></p> <ul style="list-style-type: none"> • LDH (repeat daily if elevated) • Troponin⁵ (repeat q2-3d if elevated) • Baseline ECG (QTc monitoring algorithm) <p>With clinical deterioration, repeat risk stratification labs.</p>	<p><u>If clinically indicated:</u></p> <ul style="list-style-type: none"> • Blood cultures (2 sets) if bacteria suspected • IL-6 if Category 2 or 3 risk factors • β-HCG for women of childbearing age

Table 4.5. Table from Massachusetts General Hospital (MGH) COVID-19 Treatment Guidance, Version 6.1 7/1/2020 9:00 AM.

Many important concepts emerge regarding COVID-19 from this treatment guidance.

First, Harvard discusses their work-up for diagnosis, prognosis, and risk stratification. That is, they recognize that everyone with COVID-19 is different and is uniquely positioned in the health-disease continuum.

Second, proper diagnosis requires testing for biomarkers not commonly measured in the standard of care. Note that lipids (cholesterol) testing is not even on the testing panel.

Third, viral serologies are performed. This test is not just for SARS-CoV-2. Harvard recognizes that viruses are part of our makeup and that the level of these comorbid pathogens impacts outcomes in COVID-19.

Finally, blood cultures for comorbid bacteria are also performed “if clinically indicated” or “if bacteria suspected.” Elevated neutrophils provide the clue that bacterial infections are activated.

We can learn from the pandemic experience. The most important teaching points are:

- First, the virus must be treated early, not just during hospitalization.
- The immune response storm (cytokine storm) must also be quelled. And,
- Stealth infections, lying in wait, must be tested for and treated. If they cannot be specifically identified, immune cell biomarkers like elevated neutrophil counts provide adequate justification for treatment in a crisis.

White blood cell counts play an important role in understanding diseases, including those caused by SARS-CoV-2.

WBC Count Conclusions

Thousands of medical research articles discuss the topic of white blood cell count, early death, and disease. For example, a PubMed search of “leukocyte” and “mortality” brings up 462,000 distinct journal citations. The most important conclusion to draw from this section is that the WBC count is very easy and inexpensive to obtain and provides significant information about your current and future health. However, this assumes the person interpreting the value for this marker understands the true normal range and the consequences of an abnormal value.

The numbers that modern medicine assigns to “normal” (interpreted as “healthy” ranges) are DEAD wrong. So what is the “high” WBC count of concern? The research we cite here shows that some arbitrary cut-off number does not define health. You are not healthy at a value of 5699 but unhealthy at 5700. WBC counts express a continuum of health. This is the real world.

Do worry about your numbers. Instead, focus on the causes of the numbers. Find a doctor who will dig deeper and broader into your physiology and health. To do this, you must leave the standard-of-care and the payer system to achieve real health. Say goodbye to the system that does not use science. This system was designed by a bunch of officials that do not practice medicine but arbitrarily assign normal values to prescribe reimbursable drug treatments for profit, not health.

Do not expect the standard of care published upper range of normal for WBC to change to reflect new views on its predictive value. In fact, the trend is just the opposite. The WBC normal range has regrettably expanded over the past several decades. And WBC is not the only one with an inappropriate and widening range. For example, normal uric acid used to be defined as 6.8 mg/dL or below. At that level, uric acid is soluble in your tissue. Above that value, it forms painful crystals in your joints and is diagnosed as gout. So why is the new “normal” value for uric acid 9 mg/dL? This is beyond comprehension. Your only option is to personally understand the implications of “so-called” normal values and educate yourself by

reading the medical literature, but maintain a level of skepticism, especially with recent studies mostly funded by drug companies.

Finally, what causes elevated WBC counts, and how can you be treated to reduce your risk of sudden or early disease or death?

Infections drive up WBC counts and nothing else.

Red Blood Cell Distribution Width (RDW)

RDW is more complicated to interpret than WBC because it is less specific. Red blood cell distribution width-coefficient of variation (RDW-CV or simply RDW) is a routine component of the complete blood count, automatically generated by most hematology analyzers. It is a very inexpensive test. RDW is a quantitative estimation of the heterogeneity of the volume of red blood cells (RBCs), commonly known as anisocytosis. Elevated RDW can result from increased RBC volume variance and mean corpuscular volume (MCV) reduction. However, the RDW value also reveals inflammation to those who understand the various ranges associated with the RDW value.

The diagnosis of anisocytosis means that your red blood cells are of mixed sizes. Normally, red blood cells should be about the same size, 11.5 – 12.5 percent. Highly elevated RDW values are classically associated with anemia. WebMD answers the question, “what is the RDW?”¹²⁵

“RDW stands for the red blood cell distribution width. This is a standard reported measure on a complete blood count (CBC) lab test. It measures the variability in red blood cell size.

In the normal state, red blood cells are continually being produced and removed from the blood at a steady rate. As a result, the young, immature red blood cells are larger than mature red blood cells. As a result, there are predictable proportions of large and small red blood cells, which can be plotted on a graph as the normal values.

In certain forms of anemia, the RDW may be higher than normal because there are more immature or abnormal red blood cells skewing the statistical range of values.

The RDW result is nonspecific. If a doctor suspects an unusual form of anemia, there are more sophisticated tests that can make the diagnosis.”

WebMD used “the kiss of death” term for RDW – “nonspecific.” Nonspecific means the marker goes up in many conditions. In standard-of-care lingo, doctors do not have a particular drug to treat elevated RDW. This creates a problem for medical providers as there is no expedient way to lower RDW. Instead, they prefer convenient diagnoses like “cholesterol,” so they can quickly prescribe a pill and send you on your way, often to poorer health. Sixty percent of Americans have at least one chronic condition for a reason.

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Nonspecific, however, is what chronic diseases are. Governments, societies, consensus groups, and insurance actuaries come up with disease categories. The chapter on immunity shows that only five types of white blood cells are defending our health – yet there are ~70,000 named diseases in the 2020 coding book ICD-10. We do NOT have ~70,000 different types of immune responses! The 1979 ICD-9 code book was established with just ~14,000 diagnostic codes. Since 1979, have 56,000 new disease-fighting mechanisms been discovered in humans, or have there been 56,000 new drugs marketed? In 2022, there are over 20,000 drugs approved for marketing by the FDA, and more flow into the medical system daily. The point is that almost every chronic disease overlaps with respect to our immune system's response. Who is right, ICD-10 or immunity?

Non-specific markers are a blessing, especially if there are ways to improve them with interventions, including lifestyle. Imagine lowering your RDW value and, at the same time, lowering your risk for heart disease, cancer, diabetes, and Alzheimer's. Who would be against that other than our sick-care health system?

Upon careful review of the science behind the “life and times” of red blood cells, four health ranges emerge for this biomarker: low, optimal, inflammation, and anemia. Yet, inexplicably, the inflammation range is not considered in the standard of care, and current reference ranges for RDW consider the inflammatory range “normal” Figure 4.9.

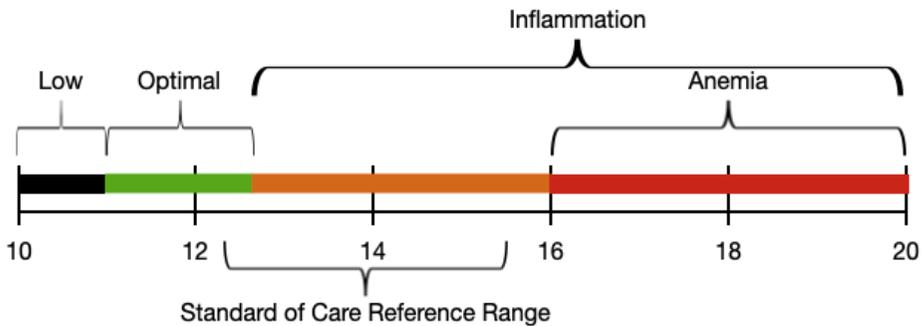


Figure 4.9. Red Blood Cell Distribution Width (RDW) ranges by percent. The ranges are low (black region), optimal (green region), inflammation (orange and red regions), and anemia (red region).

RDW is a profound indicator of your current health risk and future prognosis. It is an indication of vessel health. The inflammatory marker C reactive protein (CRP) in the inflammation zone is usually elevated above the scientific "normal value" by approximately the same amount as the RDW. CRP is a protein made by the liver and sent into the bloodstream in response to inflammation. Therefore, the test pair is quite indicative of the health of your capillary vessels, Figure 4.10.

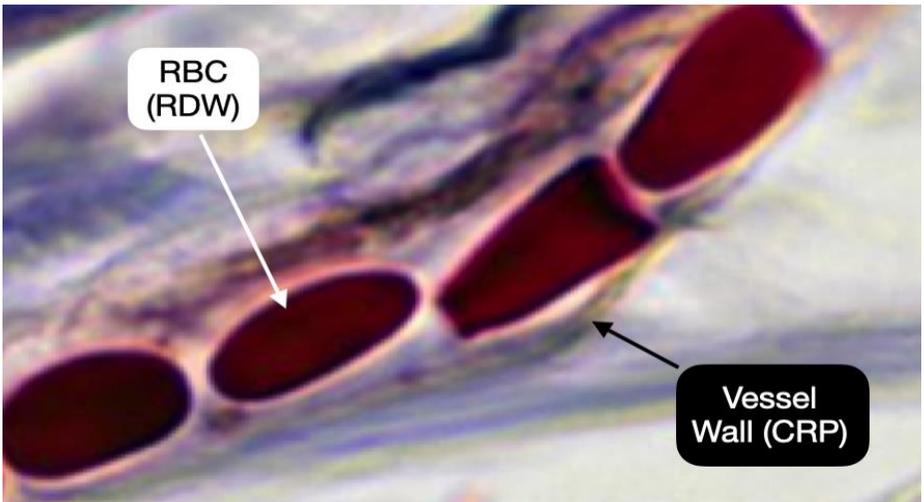


Figure 4.10. Red blood cells move single-file through a capillary. The biomarker, CRP and RDW elevate with inflammation within the vessel.

Anemia is not a deadly disease. However, mortality risk sweeps up sharply with increasing RDW, Figure 4.9. Figures 5.11A and B are from two completely different studies. The trend is clear that a higher RDW value predicts higher mortality. Since anemia is not responsible for the elevation in early mortality, inflammation and associated chronic infections are the logical causes. The WBC test can confirm this connection.

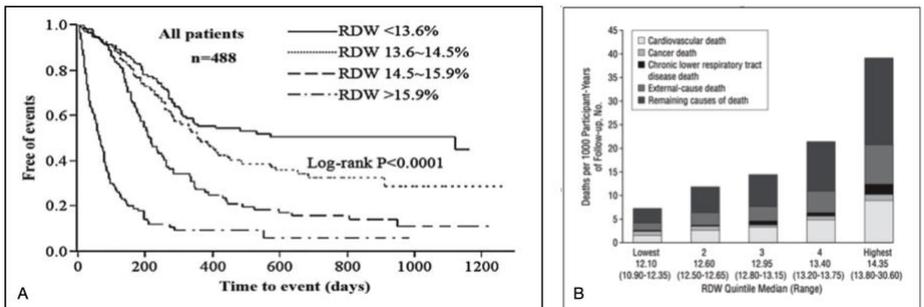


Figure 4.11A. Survival curves for mortality rates from all causes and hospital re-admission stratified according to red blood cell distribution width quartiles among 488 patients.¹²⁶ Rates of reaching endpoints were significantly higher among those with higher red blood cell distribution width, and the data meets statistical validation criteria.

Figure 4.11B. Association of red blood cell distribution width (RDW) with mortality in the Third National Health and Nutrition Examination Survey (NHANES III).¹²⁷ Rates of all-cause, cardiovascular, cancer, and chronic lower respiratory tract disease deaths increase 500% from the lowest to highest RDW quintile.

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A complete blood cell count with differential includes the RDW data. However, since it is viewed as an anemia marker, doctors look at the value to see if it is in the anemia zone. That is, it is either viewed as normal or high for anemia without regard for what this biomarker is actually conveying. Elevated RDW is a strong indicator of vascular inflammation and the risk of dying young.

A group from Beijing explains why RDW values define a continuum of risk for early mortality, at least in the standard of care speak. In their paper, "High red blood cell distribution width is closely associated with risk of carotid artery atherosclerosis in patients with hypertension,"¹²⁸ they explain that "RDW is associated with adverse cardiovascular outcomes. Elevation in RDW was tracked linearly with carotid artery atherosclerotic plaque and carotid intima-media thickness (IMT) to inner diameter ratio." These measurements determine the degree of atherosclerosis (hardening of the arteries). Not surprisingly, they also showed that increases in white blood cell count were a significant and independent contributor to the RDW elevation. This connection substantiates that the process of heart disease is infectious as that is what stimulates the inflammatory immune response.

Indeed, RDW is known within the medical research community as an indicator of various chronic diseases, with cardiovascular diseases leading the list. A PubMed search that included the "red blood cell distribution width" in the "title only" yielded 445 articles. Many of the articles discuss the association between RDW and disease. About 42% of the articles link abnormal RDW and cardiovascular diseases, and 15% associate abnormal RDW with early mortality. Table 4.6 shows that this test is reasonably specific for cardiovascular disease risk and that when RDW is abnormal, many other disease types may crop up. This table further illustrates the connectivity of diseases and shows that the WebMD statement that this is a test for anemia is WAY OFF BASE.

Disease or Indication	% Of Articles
Mortality (all-cause)	14.90%
Cardiovascular Diseases	42.00%
Cardiovascular disease (non-specific)	14.90%
Heart Failure	7.21%
Heart attack	4.81%
Acute coronary artery syndrome	4.33%
Stroke	3.85%
Thrombocytopenia	2.88%
Hypertension	2.40%
Atrial fibrillation	0.96%
Carotid artery atherosclerosis	0.48%
Total – cardiovascular diseases	41.82%
Anemia	11.54%
Metabolic syndrome	3.85%
Inflammation	3.37%
Iron deficiency	3.37%
Kidney function	2.40%
Liver disease	1.92%

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Disease or Indication	% Of Articles
Rheumatoid arthritis	0.96%
Cancer	0.96%
Acute infection	0.96%
TSH – thyroid function	0.96%
Sepsis	0.96%
Poor functional status	0.96%
Brain injury/head trauma	0.96%
COPD	0.96%
Dyspnea (shortness of breath)	0.96%
Blood (hematologic disease)	0.48%
Microcytosis	0.48%
Capillary velocity	0.48%
Tuberculosis	0.48%
Hematuria (blood in urine)	0.48%
Hepatitis B	0.48%
Bone marrow stimulation	0.48%
Membrane integrity	0.48%
Lupus erythematosus	0.48%
HIV	0.48%
Vitamin B12 deficiency	0.48%
Obstructive sleep apnea	0.48%
Crohn’s disease	0.48%
Ulcerative colitis	0.48%
Smoking	0.48%
Lung cancer	0.48%
Acute appendicitis	0.48%
COVID-19	7.19%

Table 4.6. Abnormal red blood cell distribution width and associated diseases based on a review of 445 published articles.

Since the onset of COVID-19, 32 scientific articles on the association between RDW levels and COVID-19 outcomes have been published using a title-only search. That constitutes 7 percent of the total number of references on RDW when using the same search strategy. RDW is a logical biomarker to measure COVID-19. SARS-CoV-2 infection can cause direct injury to the peripheral circulating RBCs or erythroblasts in the bone marrow and an indirect injury to RBCs due to hemolytic anemia or intravascular coagulopathy and disturbances in iron metabolism.

The spike protein has been shown to physically damage cells, specifically red blood cells, leading to the elevation of the D dimer clotting biomarker. Elevated RDW for COVID-19 patients admitted to a hospital portended higher mortality. In a report of 622 hospitalized individuals, death rates jumped 100 percent when RDW was >14.5% compared to those with lower RDW values.¹²⁹ In the article, the author state, “Of the 97 patients with a fatal outcome, 53% (51/97) had an elevated RDW on admission, and 47% (46/97) had a normal RDW (P <.001).”

The study used the standard of care normal value for RDW. This data implies that the RDW value of >14.5 is well above a true scientific normal value. Comparing groups above and below 14.5, both levels include people in the inflammation

zone. And a major cause of death in COVID-19 is a cytokine storm. This is a fancy term for high inflammation. Those who died but had an RDW of $<14.5\%$ may have had different complications compared to the $>14.5\%$ group. However, RDW cannot be excluded as a contributor to death because of the unscientific interpretation of RDW's normal values. This is further evidence for the need to view biomarkers on a continuum rather than in groups encompassing broad ranges of a biomarker.

The madness continues. In a trial including 1641 patients with COVID-19, RDW was associated with an increased mortality risk of 100 percent.¹³⁰ Two RDW ranges, $>14.5\%$ versus $\leq 14.5\%$, were used. In a group of 294 hospitalized COVID-19 patients, RDW was associated with increased mortality of 450% after adjustment for age, anemia, and co-morbidities. Two RDW ranges were used in this analysis, $\leq 14.6\%$ versus $>14.6\%$.¹³¹

Another obvious problem emerges when non-science-based “normal” values are used to draw conclusions from research studies. When the true normal value for RDW is not known or appreciated, studies end up comparing sick people to other sick people rather than sick to healthy people. The data, therefore, is not representative of actual risk. Thus, medical research will present much lower presumed risks for the elevation of the biomarker because of this important error. As a result, medicine will not advance in understanding chronic conditions, in particular.

Here is a summary of a few key published studies to support the assertion that the RDW biomarker predicts early mortality.

A Harvard Medical School and Harvard School of Public Health team published "Red blood cell distribution width and mortality risk in a community-based prospective cohort." ¹³² Their conclusion is simple (sort of):

“Higher RDW was associated with increased mortality risk in this large, community-based sample, an association not specific to CVD. Study of anisocytosis may yield novel pathophysiological insights, and measurement of RDW may contribute to risk assessment.”

They also state:

“The highest quintile (5 groups) of RDW, compared with the lowest, was significantly associated with 134% increased risk of cardiovascular mortality after multivariable adjustment” and

“The highest quintile of RDW, compared with the lowest, was significantly associated with an 88% increased risk of death due to cancer.”

It is interesting but not unusual to see one biomarker, in this case, RDW, associated with both cancer and cardiovascular disease. This type of clear correlation indicates that the diseases share similar root causes.

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Red blood cells do not form into “abnormal” sizes without reason. So what could the cause(s) of this abnormality be? Well, both cancer and cardiovascular diseases are chronic diseases. And we started this book by saying inflammation is at (or, more correctly, close to) the root of all chronic diseases. So it should be no surprise that the Harvard team found “a possible role for inflammation.” Here is what Harvard had to say:

“We hypothesized that the association of RDW with mortality risk may be due to underlying inflammation, as inflammation is increasingly appreciated to contribute to the pathogenesis of the chronic disease. Our data support an association of anisocytosis with inflammation and suggest that the association of RDW with mortality risk may, in part, be due to an effect of inflammation on both anisocytosis and risk. However, we did not find that the association of RDW with mortality risk is entirely dependent upon inflammation, as the risk associated with RDW was not significantly diminished in participants with a low CRP level compared with those with a high CRP level.”

The Harvard group is making a slight misinterpretation of their measurement of inflammation. Measuring CRP is a very good way to measure inflammation, but it is not the only way. CRP is a measure of vascular inflammation specifically. White blood cell counts and measurements for infectious species should be included in a complete evaluation of inflammation causes.

Three important lessons emerge from this elegant study:

1. First, abnormal RDW is a strong predictor of future deadly chronic diseases.
2. Inflammation is associated with abnormal RDW.
3. The correlation in 2. above is not absolute; thus, no single test, either CRP or RDW, is definitively predictive as a stand-alone test.

Patients can help our understanding of physiology by demanding more robust (deeper and broader) testing. Demanding better tests is the concept of “pull-through” marketing. If enough educated people ask for important tests not routinely performed, maybe healthcare will do the right thing for our children, if not us, and make tests and interpretations like that presented here for WBCs and RDW more available. But you have to ask. You have to become involved. Expect your doctor to say, “I cannot justify those tests.” However, curious doctors may look into these alternative tests and start conversations with colleagues.

Hope springs eternal.

Harvard Medical School does not hold exclusive knowledge on the RDW, disease, and early death connection. What follows is a short list of research titles on this topic and includes their affiliations:

“Red cell distribution width as a novel prognostic marker in heart failure: data from the CHARM Program and the Duke Databank.”¹³³ Duke Clinical

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Research Institute, Durham, North Carolina; London School of Hygiene and Tropical Medicine, London, United Kingdom; University of Glasgow, Glasgow, United Kingdom; Brigham and Women's Hospital, Boston, Massachusetts; McMaster University, Hamilton, Ontario, Canada; AstraZeneca LP, Wilmington, Delaware.

“Relation Between Red Blood Cell Distribution Width and Cardiovascular Event Rate in People with Coronary Disease.”¹³⁴ Department of Medicine, Division of Nephrology, University of Alberta, Alberta, Edmonton, Canada; Harvard School of Public Health, Boston, Mass; London Health Sciences Center, London, UK; University of Texas School of Public Health, Austin; and Brigham and Women's Hospital, Boston, Mass.

“Red cell distribution width and mortality in predominantly African-American population with decompensated heart failure.”¹³⁵ Detroit Medical Center at Wayne State University, Detroit, MI.

“Red blood cell distribution width and the risk of cardiovascular morbidity and all-cause mortality: a population-based study.”¹³⁶ Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, Medical division, Maccabi Healthcare Services, Tel Aviv, Israel.

“Red Blood Cell Distribution Width and Risk of Cardiovascular Events and Mortality in a Community Cohort in Taiwan.”¹³⁷ Prof. Yuan-Teh Lee, Department of Internal Medicine, National Taiwan University Hospital, 7 Chung Shan South Road, Taipei 100, Taiwan.

“Increased Red Blood Cell Distribution Width Associates with Cancer Stage and Prognosis in Patients with Lung Cancer.”¹³⁸ Respiratory Center, Shinko Hospital, Kobe-city, Hyogo, Japan.

“Red cell distribution width: an inexpensive and powerful prognostic marker in heart failure.”¹³⁹ Department of Cardiology, Division of Cardiovascular and Respiratory Studies, Postgraduate Medical Institute, Castle Hill Hospital, Kingston-Upon-Hull, East Yorkshire, UK.

The RDW biomarker predicts adverse outcomes across a broad range of diseases. It is a strong indicator of underlying inflammation and infection. Do not expect to get an evidence-based explanation of RDW from the standard of care. Thus, arm yourself with the information provided here, evaluate your own RDW level, and seek further testing into the cause of the inflammation, emphasizing chronic infections.

Overhaul 2. Breadth of Biomarkers

Biomarkers matter, with emphasis on the plural. A single biomarker does provide information, but the value may be confounded due to several factors that make using one or only a few markers dangerous when it comes to health decisions.

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Putting exorbitant emphasis on a single biomarker, cholesterol, for example, has much to do with the poor state of health in the United States and globally.

Health is a journey, thus a story about all your life circumstances and experiences. When read and interpreted properly, multiple labs tell the story of your health rather than just providing a snapshot. Understanding the influence of biomarkers on the story of health requires the interplay of science and clinical observations. Clinical observations do not contribute to new knowledge about the biomarker if a lab is never or seldom run. Just looking at lipid numbers and concluding that your “cholesterol” is too high is expedient, ignorant, and usually incorrect.

Using and interpreting multiple biomarkers to predict disease and early mortality is surprisingly uncommon, even in medical research. It is much easier to do a study and draw conclusions on the impact of a single biomarker. Studies asserting the value of a single value on the health of complex organisms like humans are naïve. Biased or incomplete data led Dr. John Ioannidis, Chaired Professor at Stanford Medical School to write the paper titled “Why most published research findings are false.”¹⁴⁰ Medical research, distinct from clinical delivery, delves into areas of medicine, most of which seldom reach doctors. An NLM search of “blood biomarkers” and “multiple” yields a scant 62 references.

The article “Predicting mortality with biomarkers: a population-based prospective cohort study for elderly Costa Ricans” is an example of a study using multiple biomarkers.¹⁴¹ The article's conclusion is poignant in illuminating how important biomarkers that predict health and survival are seldom obtained. According to Rosero-Bixby and Dow, the authors:

“Medicine needs a deeper understanding of the meaning of some biomarkers in elderly populations and outside of the developed country settings, where they have been primarily studied. Given this lack of information, we cannot tell whether the results found for elderly Costa Ricans are a peculiarity of this country, whose adult population has an exceptionally high life expectancy, or whether they may be extrapolated to other adult populations in the developing world.”

The biomarkers highlighted in their study are common but not commonly drawn by your doctor. They include; high-sensitivity C reactive protein (CRP), HbA1c, and DHEAS, a steroid. C reactive protein is a marker of inflammation and costs less than 3 dollars to obtain. Few doctors will order a CRP test even if a diagnostic code exists. They do not have a drug to lower an elevated value. There is startling insufficient data on CRP from the United States and global populations to draw conclusions beyond the narrow Costa Rican population studied.

Cancer is a disease in which multiple biomarkers have been evaluated more frequently than other diseases. An NLM query of “multiple biomarkers cancer” yields 198 separate peer-reviewed titles. In one rather typical example, the biomarkers used in the study were not common or affordable. For example, in the

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report titled “The prognostic factors and multiple biomarkers in young patients with colorectal cancer,” the biomarkers used were: PRL, Wrap53, RBM3, DNA status, TAZ, D2-40, Apoptosis, Fibrosis, Microsatellite status, SPF, Cox-2, p73, PINCH, Necrosis, CD163, Ki-67, FXYD-3, NFKB, Mac30, p53, Inflammatory infiltration, AEG-1, c-erbB-2, and ras.

You will not be getting this panel at Labcorp or Quest.

The neutrophil-to-lymphocyte ratio (NLR) is a cancer biomarker critically important to measure in everyone. Unfortunately, it is not considered in most multiple biomarker studies on cancer. This test costs less than 2 dollars and is predictive of cancer risk and prognosis. However, the NLR may not be sufficiently fancy or novel. And it has not found its way into clinical practice. Only one paper out of millions includes the NLR and all-cause cancer mortality. However, there are sufficient studies on NLR and cancer outcomes to validate its high predictive value.

A key NLR report, “Usefulness of the Neutrophil-to-Lymphocyte Ratio in Predicting Short- and Long-Term Mortality in Breast Cancer Patients,” asserts that

“NLR is an independent predictor of short- and long-term mortality in breast cancer patients with NLR > 3.3.”¹⁴²

The standard of care does not have a reference range of normal for this biomarker, but we provide a science-based normal range in Chapter 5.

The NLR biomarker is powerful for three important reasons.

1. NLR reflects an innate immune response. Neutrophils and lymphocytes are types of white blood cells, the primary function of which is to identify and destroy infections.
2. NLR is predictive and prognostic across most solid tumor cancers and other diseases, not just cancer.
3. NLR is extraordinarily inexpensive, often costing less than 2 dollars.

Even though the NLR is highly predictive of disease and outcome in many instances, it is still limited. After all, it is a combination of just two biomarkers. Basic physiological mechanisms, not ICD-10 codes, drive disease processes. These mechanisms fall under several categories. Specific biomarkers help explain the risks conveyed within a given category. Often, a single biomarker may change within different categories. Such markers are referred to as “non-specific.” Although labeled as unique in the coding system, chronic diseases are also non-specific. As it turns out, these non-specific markers are often highly predictive of health outcomes.

Obtain so-called non-specific biomarkers whenever you can. These are common biomarkers that are not commonly obtained.

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Disease categories refer to mechanisms or drivers of potential degeneration and disease. The major categories include:

- Metabolic – improperly measured. Fasting insulin must always be obtained. A1C must not be used to make therapeutic decisions because it is a backward, not a forward-looking, biomarker.
- Immune Function – seldom measured. Vitamin D is at the top of this list.
- Inflammation – rarely measured. Hs-CRP, fibrinogen, and uric acid are examples.
- Chronic Infection – rarely measured. Oral pathogens, Lyme disease, and chlamydia pneumoniae are tests to obtain.
- Oxidative Stress – seldom measured. Iron parameters, including ferritin, and isoprostanes, illuminate oxidative stress.
- Tissue Damage – rarely measured. Creatine kinase and lactate dehydrogenase are useful tests.
- Clotting – seldom measured. In this category, there is clotting and clumping. The erythrocyte sedimentation rate measures clumping, whereas D-dimer measures clotting.
- Hormones – seldom measured. Did you know that the actual cholesterol molecule (not LDL or HDL) is the base molecule of most hormones, including testosterone, estrogen, cortisol, and the prohormone vitamin D? This is yet another reason to leave your lipid levels untouched by drug treatment.
- Deficiencies – infrequently measured. The erythrocyte sedimentation rate is a measure of nutrient absorption. Other tests include RBC magnesium, homocysteine, ferritin, and iron.

The tests provided within each category are an example, and more biomarkers must be obtained within each category to more completely determine the contribution of each of these categories to health. This approach may, at first, appear expensive. Not every biomarker needs to be obtained on every person. A subset of markers may be used as a screening tool. If certain biomarkers are elevated, more testing may be performed to improve the quality and accuracy of a diagnosis and treatment. Regardless, when it comes to obtaining more biomarkers compared to the current broken model, cliché like “a stitch in time saves nine” could not be more relevant. Koreans, for example, focus on broader testing and prevention and consequently pay 1/4th for healthcare compared to Americans while living five years longer. Korean society is experiencing the largest increase in lifespan compared to any other developed nation. The cliché is true!

The standard of care allows for very limited biomarkers that doctors can order without a diagnosis. The reasons behind the use of this panel are complex and difficult to pinpoint. However, retro synthesizing the process brings clarity. The typical doctor visit includes

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- a blood pressure measurement. White coat syndrome often causes blood pressure to be elevated. Regardless, drugs are prescribed with even marginally elevated blood pressure.

In the case of blood pressure interventions, most doctors do not even follow the standard of care. The guidance for slightly elevated blood pressure includes a second measurement and a 24-hour home monitor if the first and second in-office values are elevated. Do you or someone you know get the home monitor of the prescription?

- A lipid or "cholesterol" test. Note the actual cholesterol molecule is NOT included in the cholesterol test. When the lab results are final, the likelihood of being prescribed a statin drug is very high. Healthy people rarely have an LDL below 100, and the chances of being below the ACC preferred level of 70 mg/dL are close to nil. But, the pressure to take the drug is strong.
- An A1C or glucose test. Metformin is frequently prescribed. However, type 2 diabetes is a highly reversible lifestyle disease. Sadly, meaningful lifestyle discussion rarely occurs.

Way too many people are put on the “big three” blood pressure medication, metformin, another diabetes drug, and statin. It is based on inadequate data and improper interpretation of the limited data obtained. This is not health freedom.

Mood drugs are fast becoming the number one most prescribed pharmaceutical class. Many people convey that their doctors recommend such drugs when they express anxiety over a health condition that persists. During the COVID-19 pandemic, recommendations for mood drugs in otherwise healthy people were common. There are no lab tests, at least in the standard of care, to assert the need for a mood drug. Thus, prescribing these drugs is completely subjective and unscientific. According to PsychCentral,¹⁴³

“There are currently no lab tests to predict or determine the best antidepressant for you. Although the test-to-prescribe science is still in development, obtaining blood work as part of mental health assessments and treatment may still be important.”

Do you find it troubling that there is little science behind this highly prescribed class of drugs?

Chronic vs. Acute Measurements

Chronic disease measurement is of utmost importance as chronic conditions drive 90% of adverse health. And, in most cases, smoldering chronic conditions eventually result in apparent “acute” adverse health events. Oddly enough, chronic disease status is best measured with so-called “acute phase reactants” and “acute phase proteins.” Testing for substances that reflect immune health status and response is key for measuring resilience and response to chronic insults. The

term “insult,” as a medical term, means “the cause of some kind of physical or mental injury.”

Acute phase reactants (APR) or proteins (APP), collectively referred to as acute phase substances (APS), are markers that exhibit changes in serum concentration during inflammation. These are important mediators produced in the liver during acute and chronic inflammatory states. In acute disease, the changes in these markers are significant and may even exhibit values outside the standard of care reference ranges, but not always. The sepsis example earlier in this chapter explains that the WBC counts may be “normal” in some instances of sepsis.

Contrary to acute diseases, in chronic diseases that matriculate slowly and continue to fester over a long time, these markers change slightly and slowly, either up or down. The slight alterations in biomarkers reflect the level of smoldering disease ongoing in your physiology. In this circumstance, lab values never exceed current reference ranges until “too late.”

APSs can be classified as positive or negative, depending on their serum concentrations during inflammation, according to authors of “Physiology, Acute Phase Reactants.”¹⁴⁴ “Positive acute phase reactants are upregulated, and their concentrations increase during inflammation. Negative acute phase reactants are downregulated, and their concentrations decrease during inflammation. Positive acute phase reactants include procalcitonin, C-reactive protein, ferritin, fibrinogen, hepcidin, and serum amyloid A. Negative acute phase reactants include albumin, prealbumin, transferrin, retinol-binding protein, and antithrombin.” Other markers can go either way. Examples are uric acid, WBC counts, neutrophils, and lymphocytes. Unfortunately, some of these markers are not practical to apply to populations because of the paucity of data on them or expense.

White blood cells (WBC), also called leukocytes, are the key innate immune biomarkers that change with some type of infection. Certain harsh treatments, including chemotherapy and biological drugs, can impact the health of bones and liver, thus changing WBC values and, therefore, must be considered when evaluating WBC levels. Combining white blood counts with APSs enhances diagnostic accuracy and aids in determining the source or type of insult.

Since the innate immune system responds to infection, measuring specific infectious species must be considered for inclusion in lab panels for measuring chronic disease. However, the WBC values may be used to determine if such tests are necessary. Optimal WBC counts indicate that any infection, if present, is inactive. Although a crisis like the pandemic of 2019 created awareness of acute infections, chronic infections that cause smoldering chronic diseases are much more prolific but seldom considered in laboratory evaluations.

Interleukins (IL) are a type of cytokine first thought to be expressed by WBCs alone but have later been found to be produced by many other body cells. They

play essential roles in the activation and differentiation of immune cells, as well as proliferation, maturation, migration, and adhesion. These substances fall under the general classification of APSs. Nevertheless, interleukins are seldom part of an initial lab workup. One reason is their relatively high cost.

Hormones are regulatory substances and are measurable biomarkers. Hormones are signal molecules or chemical messengers. They travel throughout the bloodstream to tissues or organs. The cortisol hormone responds very rapidly, for example, to elevated blood pressure under a physical stressor. It regulates the "fight or flight" response. Some hormones function slowly over time and affect many processes, including growth and development, metabolism, sexual function, reproduction, and mood. They also control many other physiological processes indirectly. Very small amounts of hormones are capable of causing big changes in cells with repercussions throughout the body.

Vitamin D is a pro-hormone, not a vitamin. It is produced photochemically in the skin from 7-dehydrocholesterol. The molecular structure of vitamin D is closely allied to that of classic steroid hormones (e.g., estradiol, testosterone, cortisol, and aldosterone) in that they have the same root, the cholesterol molecule - not to be confused with "total cholesterol." Total cholesterol is a complete misnomer as it is the aggregated of lipid (fat) molecules, specifically low- and high-density lipoproteins and triglycerides. Generally, prohormones are converted by an enzymatic process into anabolic hormones, which help generate protein synthesis and stimulate muscle growth. "Vitamin D" regulates cell division. This is one reason why it is protective against cancer.

The RDW biomarker is particularly useful for distinguishing between acute and chronic disease processes. The concept of biomarker half-lives is not well appreciated or studied. C-reactive protein has a half-life of about 1.5 days. This means if CRP suddenly elevated due to trauma, for example, its value will decrease by one-half every day and a half. If CRP is elevated by an underlying chronic process, it will stay elevated. However, when labs are obtained infrequently, one cannot be certain if it is due to an acute (trauma) or chronic reason.

Red blood cells measured in the RDW biomarker are replaced every 4 months. The RDW half-life is much longer compared to CRP. This means it goes up and down more slowly compared to CRP. And CRP and RDW are often measures of the same inflammation source. Therefore, if CRP and RDW are elevated to the same extent, the most likely reason is a chronic process. Therefore, multiple biomarkers afford superior diagnostic assessment of health for two reasons.

- Increasing the number of biomarkers increases the precision and accuracy of a measurement.
- Biomarkers often have different half-lives, which help differentiate between acute and chronic disease processes.

Essential Biomarkers

The depth and breadth of biomarkers are important considerations when making a diagnosis. Table 4.7 provides a list of essential biomarkers, the standard of care reference ranges, and the science-based reference ranges.

Biomarker†	Standard of care normal	Evidence-based normal
A/G Ratio	1.2 - 2.2	Same ^c
AIP ^c	Not Established	<0.12
Alkaline Phosphatase	44 - 121 IU/L	45 - 100
ALT (SGPT)	0 - 44 IU/L	10 - 32
Antinuclear Antibodies (ANA)	Negative	Same
AST (SGOT)	0 - 40 IU/L	10 - 26
Basophils (Absolute)	0.0 - 0.2 per mL	Same
Bilirubin, Total	0.0 - 1.2 mg/dL	Same
BUN	8 - 27 mg/dL	Same
BUN/Creatinine Ratio	10 - 24	Same
C-Reactive Protein	0 - 3 mg/dL	<0.6
Creatine Kinase, Total	41 - 331 U/L	32 - 150
Creatinine	0.76 - 1.27 mg/dL	Same
D-Dimer	0 - 0.49 mg/L FEU	<0.21
eGFR If African Am	>59 mL/min/1.73	90 - 120
eGFR If Non-African Am	>59 mL/min/1.73	90 - 120
Eosinophils (Absolute)	0 - 400 per uL	Same
ESR (Sedimentation Rate)	0 - 30 mm/hr	<3
Ferritin, Serum	30 - 400 ng/mL	30 - 120
Fibrinogen Activity	193 - 507 mg/dL	185 - 285
Gamma-glutamyl transferase	0 - 65 IU/L	<20
Glucose (Fasting)	65 - 99 mg/dL	65 - 83
Hemoglobin A1c	4.8 - 5.6%	4.3 - 5.0
High-Density Lipoprotein	>39 mg/dL	>50
Homocysteine	0 - 17.2 umol/L	5 - 10
Immature Grans (Abs)	0 - 100 per uL	Same
Insulin (Fasting)	2.6 - 24.9 uIU/mL	1.3 - 4
Iron, serum	38 - 169 ug/dL	Same
Lactate Dehydrogenase (LDH)	121 - 224 IU/L	120 - 284
Lipids, Total, Calc ^a	100 - 169 mg/dL	200 - 260
Low-Density Lipoprotein	0 - 99 mg/dL	100 - 200
Lymphs (Absolute)	700 - 3100 per uL	1400 - 2000
Lymphs %	Not determined	35 - 45
Monocytes (Absolute)	100 - 900 per uL	Same
Neutrophils (Absolute)	1400 - 7100 per uL	2000 - 3000
Neutrophils %	Not Established	52 - 58
NLR ^b	Not Established	0.6 - 1.5
RDW %	11.6 - 15.4	11 - 12.5
Triglycerides	0 - 149 mg/dL	30 - 90
TSH	0.45 - 4.50 uIU/mL	0.45 - 1.5
Uric Acid	3.8 - 8.5 mg/dL	3.5 - 6.0
Very Low-Density Lipoprotein	5 - 40 mg/dL	5 - 24
Vitamin D, 25-Hydroxy	30 - 100 ng/mL	55 - 100
WBC	4200 - 11,000 per uL	4000 - 5700

Table 4.7. List of important biomarkers for measuring chronic health and disease risk. The term "same" does not mean that the evidence-based normal value for that marker is necessarily the same as that published by the standard of care. Either there is insufficient data to establish a true evidence-based normal range, or the biomarker has not been investigated as of the publication date of this book.

†Certain comprehensive metabolic biomarkers are not included on this list because they are more indicative of acute health than chronic ones.

^AIP stands for the Atherogenic Index of Plasma.

^Lipids, Total, Calc is commonly known as total cholesterol. Since it is a measure of three lipids, the cholesterol name is inappropriate.

*NLR stands for the neutrophil-to-lymphocyte ratio.

Other important biomarkers that should be obtained include comprehensive thyroid panel biomarkers, hematology biomarkers, troponin, clotting rates, and hormones. Everyone should also receive testing for common pathogens, including h-pylori, chlamydial antibodies, oral pathogens, and spirochetes (Lyme) blot. These tests are tier 1 testing only and is adequate for determining a person's position on the health disease continuum. Further testing may be required to determine why a person is experiencing poor health.

Multiple Biomarkers and Risk Scores

Interpreting the interplay between multiple biomarkers is often daunting for the uninitiated. However, your health is a "story" and not a "snapshot," thus appreciating how biomarkers contribute to that story is essential to deeply understand health. A few incomplete scoring systems that aggregate the value of multiple labs into a single score have emerged. Caution, all of these scoring systems lack depth and breadth of biomarkers, so the scoring results, although easier to read, are an insubstantial improvement over single biomarkers evaluating your health and treatment needs. Risk scores help patients understand if they are making appropriate health improvements and to what extent. This data is also helpful to practitioners in designing treatment protocols.

Multiple biomarkers, in general, improve the predictive power lab panels. For example, in a study of 3209 people assessed with ten biomarkers, persons with multi-marker scores in the highest quintile (group of 5 value ranges) as compared with those with scores in the lowest two quintiles had elevated risks of death and major cardiovascular events of 4.08% and 184% respectively.¹⁴⁵ This far exceeds the predictive hazard ratio for cholesterol which varies from 89% to 125% depending upon the study.¹⁴⁶ A value of <100% means cholesterol levels are protective and stave off early mortality.

Risk-scoring systems have been used for decades. These scoring systems are not used frequently in clinical settings. Do you know your Framingham risk score? This predominant scoring system relies primarily on a "cholesterol" lipid panel. As a reminder, the total cholesterol value does NOT include the value for the cholesterol molecule. In most instances, when the total cholesterol number is outside of the standard of care reference range, mortality risk goes down. These scoring systems based on the total cholesterol number are not only inaccurate, but they are harmful and deadly when interventions are applied to lower the value.

The major scoring systems are used mainly to determine cardiovascular risk and are really designed to put you on a statin drug.

Atherosclerotic Cardiovascular Disease (VSCVD) Risk Score. Mayo Clinic and the American College of Cardiology provide websites that allow you to calculate your risk score if you have all the required data. The instructions state, “Calculate your 10-year risk of heart disease or stroke using the ASCVD algorithm published in 2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk. This calculator assumes you have not had a prior heart attack or stroke. If you have, it is recommended that you discuss starting aspirin and a statin with your doctor. Furthermore, if you have an LDL-cholesterol (so-called bad cholesterol) greater than 190, it is also generally recommended that you discuss starting aspirin and a statin with your doctor. Unfortunately, there is insufficient data to predict risk for those under 40 years of age or greater than 79 and those with total cholesterol greater than 320.”

The American College of Cardiology has a “guidelines made simple” document for managing blood cholesterol that is 22 pages long.¹⁴⁷ What they do not tell you is that no one on Earth knows their cholesterol value – no one. Instead, this is a low-density lipoprotein (LDL) management document. They call it LDL-C, with the “C” meaning cholesterol. There is no such thing as low-density lipoprotein cholesterol (LDL-C). There is low-density lipoprotein (LDL), however. LDL carries the cholesterol molecule, but since that molecule is not directly measured, no one knows the value. Your cholesterol level is a guess!

Regardless of the complete misinformation campaign on “cholesterol,” very few doctors use this tool. Either they are aware of the ACC guidance tool, or it is too much of a bother to plug the numbers to create the score. Instead, they prescribe a statin drug without consideration for all your biomarkers. For example, if your HDL is high and this value drives the total cholesterol value about the erroneous upper limit, you still get the statin. If they did follow the guidelines, substantially fewer statin prescriptions would be written. The guidance uses the term lifestyle 22 times. How many times did your doctor use that term during your last clinical visit? The very first guideline in the document states,

“A healthy lifestyle reduces risk of atherosclerotic cardiovascular disease (ASCVD) at all ages. In younger individuals, a healthy lifestyle can reduce the development of risk factors and is the foundation of ASCVD risk reduction. In young adults, 20 to 39 years of age, an assessment of lifetime risk facilitates the clinician-patient risk discussion and emphasizes intensive lifestyle efforts. In all age groups, lifestyle therapy is the primary intervention for metabolic syndrome.”

The message this guidance sends, if you are 40 and over, somehow you are different compared to a 39-year-old, and you must be put on a statin drug. You are beyond hope of making changes to your health. Translation: your doctor is too lazy or incompetent to help you improve your risk score, so they will take the easy way out – give you a drug – and blame it on your age.

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Here is another statement from the document that is sure to make you chortle or cry. "Invite the patient to ask questions, express values/preferences, and state ability to adhere to lifestyle changes and medications."

In the 20 – 39 age group, the guidance states, "Estimate lifetime risk to encourage lifestyle to reduce ASCVD risk. Consider statin if family history, premature ASCVD, and LDL-C ≥ 160 mg/dL. Unfortunately, most people with an LDL well below 160 but above 100 are threatened to take a statin drug to "protect your heart." Thus, those doctors are not complying with the letter or the spirit of the guidance.

The elements of the ASCVD risk calculator are shown in Figure 4.12.

The image shows a digital form for calculating ASCVD risk. It includes input fields for Current Age, Sex (Male/Female), Race (White/African American/Other), Systolic and Diastolic Blood Pressure, Total, HDL, and LDL Cholesterol, and checkboxes for History of Diabetes, Smoker status (Current/Former/Never), On Hypertension Treatment, On a Statin, and On Aspirin Therapy. Each input field has a small icon and a value range constraint below it.

Figure 4.12. Atherosclerotic Cardiovascular Disease (VSCVD) Risk Score elements.

The NHANES III survey was a nationwide probability sample of 39,695 persons aged two months and older. It was conducted from 1988-1994 in two phases. Phase 1 (1988-1991) and Phase 2 (1991-1994) were each nationally representative samples obtained over six years. In the six-year sample, 33,994 sample persons were interviewed, and 30,818 people were examined. The NHANES III study data is well respected and illuminating, particularly concerning the risk of dying young as the RDW value elevates.

In 2022, a publication from NHANES III data validated the importance of RDW in predicting disease while also showing how traditional biomarkers like total cholesterol do not.¹⁴⁸ The study divided the population into three groups based on the so-called "ASCVD" risk criteria. In the world of cardiology, regardless of voluminous data on biomarkers like CRP and RDW, cholesterol and blood pressure are all that matter because they have nice convenient drug treatments. The conclusion to the article is quoted here.

"Our study demonstrated that an increase in RDW greater than 14 was associated with significantly increased cardiovascular mortality in all ASCVD risk groups using the NHANES III database between 1988–1994, especially in the low and the intermediate-ASCVD risk cohort where RDW

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had the highest impact. Therefore, RDW may be a potential risk enhancer, similar to hs-CRP and in lieu of hs-CRP, especially for the intermediate-ASCVD risk population of people in the United States. An elevated RDW believed to be related to inflammatory and oxidative stress factors may become clinically helpful to further risk stratify individuals for cardiovascular mortality in conjunction with the ASCVD risk assessment. Further validation of our study results is required.”

These important points emerge from the data and conclusions of this research:

- Further validation of the results is NOT required. NHANES III has provided information on elevated early mortality risk and RDW values for over 15 years. This statement is intended to keep change from happening and to make doctors comfortable using useless markers like “total cholesterol.” The NHANES study has led to the evaluation of the relationship between RDW and health since 1990.¹⁴⁹ Inappropriately, doctors rarely discuss your RDW level but obsess over "cholesterol."
- Terms like “further validation is required” and “more studies are needed” are just medical research's language. Researchers seldom translate their findings into clinical reality. Instead, they just write more grant applications in their area of expertise. For example, if they concluded, “This is rock-solid data and must be immediately implemented clinically, and no more research is needed,” they would have just fired themselves from the research funding gravy train. They might even have to get a real job – God forbid.
- The data is blatantly clear that the risk algorithm the American College of Cardiology uses to manage your vascular health, ASCVD risk assessment, is almost useless. It does not include highly informative biomarkers like RDW and WBC. Instead, this so-called authoritative organization draws conclusions about heart and vessel health with; blood pressure, cholesterol, diabetes, smoking, statins, and aspirin consumption. They also want to know your age, sex, and race. Regrettably, none of these tests get to the root cause of vascular disease. Not identifying causes is why cardiovascular disease remains the number one killer in the United States and most other developed nations.

The ASCVD risk assessment lumps people into three groups based on the percent of calculated future risk of a vascular event: <7.5%, 7.5-20%, and >20%. The NHANES III study used a “weighted sample” of 85,323,902 patients. The data from a study of this magnitude is very reliable. Table 4.8 provides a summation of the data from this study.

ASCVD Risk Ranges

Measurement	<7.5%	7.5-20%	>20%	change
Age	47	62	74	57%

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Measurement	<7.5%	7.5-20%	>20%		change
Diabetes	3.3%	12.%	29.4%		890%
Cholesterol, Total	206	224	223		8%
Systolic BP	119	132	145		22%
Smoking	20	34	21		5%
Mortality	14.3%	45.8%	85.5%		600%
CRP	0.18	1.40	1.2		666%
RDW >14%	2.79	2.02	1.18		-279%
RDW 13-14%	2.81	1.15	1.04		-273%

Table 4.8 Risk changes based on various health parameters, including vital signs and biomarkers. Note that diabetes and age are the largest risk factors within the ASCVD risk assessment. Cholesterol is a very poor indicator of risk.

Mortality increases by 600% across the risk groups, but cholesterol increases by a meager 8% and goes DOWN within the highest risk score group! Also, from the 7.5-20% group to the >20% group, mortality increased by 187%, yet cholesterol went down.

The cholesterol king is dead. Long live the cholesterol king!

Diabetes and age are the risk factors revealed from this extensive yet limited set of data that the American College of Cardiology uses.

The marker of inflammation, CRP, went up 666%. Compare the predictive power of CRP to cholesterol at 8%. Which marker is more predictive of mortality? The answer is CRP, the vascular inflammation marker, by far.

Subtle changes in RDW are extraordinarily predictive of early death, with a published hazard ratio of 3.05 (305% increase) by going from an RDW of <13% to >14%. Recall that an RDW of 15.4% is considered normal. That RDW goes DOWN while the ASCVC risk score goes UP is all the proof you need to know that his scoring system is USELESS.

Trash the American College of Cardiology risk score. Instead, measure for diabetes risk, CRP, and RDW.

Do we really need more studies? American College of Cardiology, please take total cholesterol out of your risk calculator and replace it with WBC, CRP, and RDW as a starting point. However, adding more biomarkers further improves the precision of a risk score.

As you saw in Volume 1 for cholesterol, the ACC and their cholesterol fetish are completely wrong based on true, objective science, not data bought and paid for by the pharmaceutical industrial complex. This is not the opinion. Instead, it is supported by unbiased data.

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One of the most prestigious doctors of the modern era, Arnold Relman, MD, agrees. He states, as published in the *New Republic* magazine,¹⁵⁰

“The medical profession is being bought by the pharmaceutical industry, not only in terms of the practice of medicine but also in terms of teaching and research,” says Arnold Relman, a Harvard professor and former editor of the *New England Journal of Medicine*. His recent critique of the industry's influence in health care, published in the *New Republic*, won him and his co-author one of the top awards for magazine journalism in the United States. “The academic institutions of this country are allowing themselves to be the paid agents of the pharmaceutical industry. I think it's disgraceful.”

To further support the notion that the risk-scoring system is more about prescribing drugs than making an individual healthier, a pharmaceutical executive states, “A physician's prescribing value is a function of the opportunity to prescribe, plus his or her attitude toward prescribing, along with outside influences. By building these multiple dimensions into physicians' profiles, it is possible to understand the ‘why’ behind the ‘what’ and ‘how’ of their behavior.” For example, one drug representative is pushing the use of pharmaceuticals for every nine doctors. The proliferation of drug reps is an important fact about why prescribing usurps helping patients with their health.

The book “*Mad Medicine: Myths, Maxims, and Mayhem in the National Health Service*,” written by Dr. Andrew Bamji, digs deep into the pitfalls into which medical research has fallen. He was a consultant Rheumatologist at Queen Mary’s Hospital, Sidcup, Kent, and Director of the Elmstead Rehabilitation Unit. According to Dr. Bamji:

“Medical research has fallen into many pitfalls that compromise its integrity. These include:

1. therapeutic trials on the wrong anatomical diagnosis,
2. inappropriate attribution of effect to cause,
3. reliance on trials with inadequate power,
4. failure to continue trials long enough to observe rare side-effects,
5. failure to use the right statistical methods,
6. selection of data that fit the hypothesis (and converse exclusion of data that do not fit),
7. failure to account for potential confounders,
8. use of inappropriate endpoints,
9. reliance on flawed tests,
10. concealing of adverse events,
11. failure to explain the difference between absolute and relative risk, and

12. the inappropriate use of each statistical type to make results look better. And that is just on trial management.

There is the refusal to release raw data so that they may be subjected to independent analysis, failure to publish negative results, and data presentation in a biased fashion. Within these is the conclusion of some trials that A is equivalent to B when all that has happened is that the trial failed to prove a difference, which is not the same. Given the flaws found in so many trials, it is not surprising that there is skepticism, for much of the "evidence" is not really evidence at all."

Thank goodness there are only twelve things wrong with the clinical trial data used to make you "healthy!"

Framingham Risk Score. Based on the famous Framingham Heart Study, the Framingham Risk Score claims to provide a subject's risk of having a heart attack or dying from heart disease within ten years. However, vast data subsequent to the availability of this score demonstrates that it is a poor risk tool. "In very old people from the general population with no history of cardiovascular disease, concentrations of homocysteine alone can accurately identify those at high risk of cardiovascular mortality, whereas classic risk factors included in the Framingham risk score do not," according to De Ruijter, Wouter, et al.¹⁵¹ "Currently recommended risk scoring methods derived from the Framingham study significantly overestimate the absolute coronary risk assigned to individuals in the United Kingdom," states Peter Brindle et al.¹⁵²

The elements of the Framingham risk calculator are similar to the ASCVD calculator and are shown in Figure 4.13. Thus, this score cannot be accurate or valuable. The ASCVD calculator is considered an upgrade to Framingham. The only differences are that ASCVD adds questions about sex, race, and drug use. ASCVD is hardly an upgrade.

Age	<input type="text"/>	yr	▼
Systolic blood pressure	<input type="text"/>	mmHg	▼
Total cholesterol	<input type="text"/>	mg/dL	▼
HDL cholesterol	<input type="text"/>	mg/dL	▼
On blood pressure medication	Yes / No ▼		
Cigarette smoker	Yes / No ▼		
Diabetes present	Yes / No ▼		

Figure 4.13. Framingham risk calculator elements.

Reynolds Risk Score. According to the designers, the Reynolds Risk Score is designed to predict your risk of having a future heart attack, stroke, or other major heart disease in the next ten years. It is similar to Framingham but adds hsCRP and family information. "Introduction of hsCRP into cardiovascular risk assessments can refine the risk status of symptom-free subjects, especially among intermediate risk middle-age women," according to Móczár.¹⁵³ In another article on the Reynolds scoring system, Desai et al.¹⁵⁴ indicate there is value in adding hsCRP to the risk calculator. However, the Reynolds score still is an underestimate of cardiovascular risk. The problem, of course, is that total cholesterol values as not interpreted correctly for cardiovascular risk, and the reference range for hsCRP is not scientific.

Try as they may, two wrongs still do not make a right.

There is very little interest in adding hsCRP in risk scoring in the medical community. This is evident because the two informative papers summarized above and published ten years ago were cited just five times.

Doctors are not paying attention to facts.

Intermountain Risk Score. According to intermountainhealthcare.org, "Intermountain Risk Scores are a set of clinical decision tools that predict multiple types of patient risk, including hospital readmission, mortality, and the onset of serious medical conditions. Our physicians use these risk scores at the point of care to individualize each patient's treatment plan. Patients at higher risk may undergo additional testing and treatment to ensure they have the best possible outcomes. Conversely, low-risk patients may not need as many interventions, which results in cost savings for both the patient and the health system."

The intermountain risk score uses a complete blood count and basic metabolic profile to predict mortality. Focusing on a mortality endpoint is an important step in stratifying risk in populations. Two papers articulate this point. Article 1 is "Intermountain Risk Score, a predictor of mortality was associated with morbidity endpoints that often lead to mortality."¹⁵⁵ Article 2 is "The Intermountain Risk Score (including the red cell distribution width) predicts heart failure and other morbidity endpoints."¹⁵⁶

This scoring system is a departure from the cholesterol-based systems. Intermountain has the potential to be a valuable calculator, but its utility is only for very sick people. Everyone else is lumped into a general "healthy" category because erroneous reference ranges are used for the score. Also, many of the markers found on a metabolic profile panel have little to do with chronic disease but are important in a hospital setting. The markers that constitute the Intermountain score include Hematocrit, White Blood Cell Counts, Platelet, Mean Corpuscular Volume, Mean Corpuscular Hemoglobin Concentration, Red Cell

Distribution Width, Mean Platelet Volume, Sodium, Potassium, Bicarbonate, Calcium, Glucose, Creatinine, being older than 17, and being female or male.

Evaluating the various risk scoring systems demonstrate that adding measurements, particularly those associated with inflammation and infection, namely hsCRP, white blood cell counts, and red blood cell distribution width, improve the predictive capability of the risk score. Regardless, these systems lack depth and breadth of biomarkers making their results wrong or inadequate. Simply put, even the best of these risk scores do not accurately predict and stratify risk for current or future morbidity and mortality.

Risk Score Based on Proper Depth and Breadth of Biomarkers

A proper risk score is derived from biomarkers' depth and breadth. When combining biomarkers into a single score, the values of each must be based on the same endpoint. Mortality is the best common endpoint for a scoring system. A list of considerations for a bona fide risk score is provided here.

- Use of multiple biomarkers;
- Inclusion of biomarkers from a variety of risk categories;
- Harmonizing each marker to a standard endpoint - increase in early mortality risk;
- Consideration of risk contribution of each biomarker to early mortality; This is achieved by:
- Determining to what level a biomarker is elevated above or depressed below optimal scientific values and scaling the risk when the values are not optimal. According to published mortality data, risk increases log-linearly when outside of optimal levels.
- Determining the comparative "hazard ratios," that is, determining the extent to which a biomarker contributes to early mortality risk compared to other biomarkers and applying mortality risk weighting factors to each biomarker based on these published ratios.

With this scoring approach, the aggregate score is an indicator of early mortality risk and associated total morbidity burden. This single number is an important bridge to better health literacy, as most patients do not understand the meaning of their lab values. In addition, most people, including doctors, do not understand how individual markers are assembled to tell the story of their health.

A risk score does not constitute a medical diagnosis of disease more than any individual marker, like homocysteine. A properly constructed risk score affords better predictive capability and disease progression or regression measurement. A well-designed risk score can accurately define where you are on the health disease continuum.

Treatments and interventions are the most important outcome of any measurement. Knowing, for example, that CRP is elevated does not provide a

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health roadmap. That is where assessing subjective risks come in to help guide care plan development. In the case of elevated CRP, if a risk survey indicates a high intake of sugary foods or an issue with the oral cavity, like bleeding gums, then a precision care plan that addresses these risks has a high probability of lowering the CRP value. Taking a drug to lower CRP, if there was one, would not solve the food and oral issues.

Drugs seldom treat the root cause.

An important study on using a novel scoring system to use risk assessment data and lab values provides evidence that improving risks improves biomarker scores. Excerpts from the publication "Reduction in Chronic Disease Risk and Burden in a 70-Individual Cohort Through Modification of Health Behaviors"¹⁵⁷ are summarized here.

"Health risk factors, including lifestyle risks and health literacy, are known to contribute to the chronic disease epidemic. According to the Centers for Disease Control and Prevention (CDC), chronic diseases account for 90% of healthcare costs, morbidity, and mortality. In the United States, healthcare providers attempt to modulate a limited set of risks. However, chronic diseases continue to increase despite expanding wellness programs and drugs to manage and prevent chronic conditions.

Pandemics, exemplified by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), show that people in good health suffer mortality rates at 10% of that compared to those with pre-existing chronic conditions. Healthcare costs and morbidity rates often parallel mortality rates. New root-cause risk and health tools that accommodate low health literacy and are linked to personalized health improvement care plans are needed to reverse the chronic disease epidemic. Reported here is a study on 70 manufacturing employees in the Midwest of the United States using a personalized and group approach to chronic disease reversal and prevention, which may also find utility in reducing pandemic severity and may, therefore, impact policy decisions."

"Conclusion: This simple, inexpensive, root-cause-based risk and health approach generate a "do no harm" action plan that guides a care team, including the participants, on a path to improved health. The data demonstrate that changes in a novel risk calculator score coincide with changes in sensitive biomarkers for chronic disease. When an individual's risks are reduced, the biomarkers reflect that change and self-reported well-being also improves. This program and process may be of value to a society plagued with escalating levels of chronic disease and merits further study, but more importantly, immediate implementation."

"Numerous studies exist on the association between lifestyle behaviors and chronic disease risk. In large prospective studies, like the Nurses' Health

Initiative, vague conclusions are made about the association between smoking, regular physical activity, maintaining a normal body mass index, eating a healthy diet, and chronic disease proliferation.¹⁵⁸ The individualized chronic disease assessment (CDA) values potentially increase the precision, personalization, and accuracy of risk-to-disease relationship measurement. Figure 4.13 provides a view of the change in the subjective risk score and its relationship to the change in the chronic disease biomarker score at the beginning and end of a 9-month care plan intervention program for the entire population."

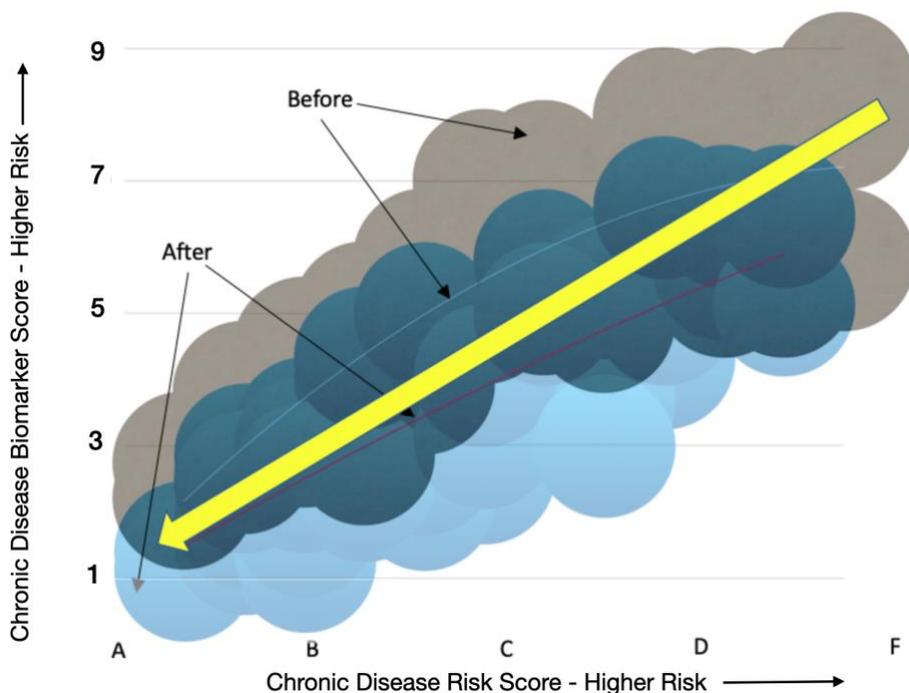


Figure 4.13. Correspondence between lifestyle risks (chronic disease risk score) and a novel blood-based biomarker score (chronic disease biomarker score) in a cohort of 70 individuals before and after precision interventions over 9 months.

The figure above illustrates a poignant example of how biomarker testing, coupled with a detailed risk evaluation, is a powerful 1-2 punch for improving individual and population health.

In this study, implementing a risk assessment, health and disease measurement, care plans, and frequent measurements leading to continuous improvement represents a needed response to the challenges society faces from chronic diseases. In addition, this “systems approach” is designed to better connect across fragmented healthcare divisions without discipline bias. That is, most chronic diseases are fundamentally connected to root-cause physiological processes, not human-defined specialty disciplines like cardiology or neurology.

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The ultimate goal is to create new risk, diagnostic, and outcome connections that facilitate learning opportunities and iterative advancement in treatment and preventative methods for chronic disease. This approach is proven to guide the process of interventions and unify different fields of medicine. For example, reversing - not managing - diabetes should be the first step in preventing heart disease, yet these diseases lie in different medical specialties. The final objective of this revolutionary change to medical delivery ensures that the medical workup of any individual patient, regardless of the presumed type of illness category, embraces all possible causal factors. The word "symptoms" is not included in this approach.

Clement Trempe, M.D. inspired this chapter's medical "workup" overhauls. He supported the value of performing an evidence-based and detailed evaluation of his patients to improve their overall health and not just treat symptoms. Dr. Trempe was often asked how he treated diseases like glaucoma and Alzheimer's because his results were superior to those obtained within the standard of care. He would tersely respond,

“Doctor, you are asking the wrong question. Instead, ask what a full and proper diagnosis is! You are a doctor thus armed with a complete, accurate diagnosis; you will know how to treat!”

"Doctors in the know understand that diseases occur because of a loss of electrons and healing occurs through a gain of electrons."

- Thomas Levy, M.D., J.D.

Electricity, Infection, and Malnutrition.

Summary: Achieving optimal health does not have to be expensive. Blood testing is a fundamental and objective way to determine an individual's health. The three tests highlighted in this chapter cost less than 10 dollars and should be used as a population health screening tool. These tests are often adequate to determine where an individual lies on the health-disease continuum. Moreover, these tests provide essential information on interventions usually sufficient to restore or optimize the individual's health without further testing.

According to Zedong, freedom is knowledge of necessity and the transformation of the world.¹⁵⁹ Foundational health knowledge allows individuals to transform and optimize their health. The history of humankind is a history of expanding knowledge. Our understanding of health has magnified, but applying that specific knowledge is being improperly directed and applied.

Authorities in charge of our medical system are suppressing knowledge about good health. It is time for a medical science-based revolution. The current system needs to change dramatically from a symptoms management process to one that addresses the root causes of disease. A majority of us are living in a perpetual state of poor health. Without revolutionary, science-based changes to healthcare testing and interventions, there can be no revolutionary improvements.

Revolutionary changes do not have to be complex or expensive. "Revolution" is "involving or causing a complete or dramatic change." We need this type of change in medicine to curb the trend in chronic diseases that impact at least 60% of the adult population in the United States. Similar developments are emerging in other developed nations.

The necessary change starts by empowering individuals with health knowledge. During COVID-19, doctors proved they could not be trusted with our health. Influential powers and bias control them. This knowledge must be provided in understandable terms and be actionable to have the most significant impact. Three steps define the new health revolution:

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1. Empower individuals with fundamental, root-cause knowledge about their health
2. Perform testing that relates to this knowledge – particularly that accessing root causes of disease
3. Provide actionable protocols that help individuals improve their health naturally. Surgeries and pharmaceuticals must be methods of last resort only.

Three (3) biomarker tests, seldom obtained currently, provide individuals with basic and fundamental root-cause knowledge about their health. Understanding, testing, and treating everyone based on these three predictive yet inexpensive biomarkers is the correct first step. These biomarkers explain health well. Each can be improved or optimized without the antiquated standard of care interventions. These three biomarkers are:

1. Fasting insulin (Insulin) – a marker of malnutrition
2. Neutrophil to lymphocyte ratio (NLR) – a marker of infection
3. Erythrocyte sedimentation rate (ESR) – a marker of electricity

Using the standard of care guidelines, doctors rarely test for these biomarkers. And, when they do, the results are almost always interpreted as being “normal” as the ranges are completely unhelpful. The ranges are part of the current sick-care system; thus, they are only “abnormal” when you are severely ill.

The previous chapter explained the concept of the health-disease continuum and how the standard of care reference ranges are not based on science. Instead, they reflect the current health of our unhealthy population. Table 4.1 shows the three critical biomarkers, the standard of care reference ranges, and the science-based reference range based on premature all-cause mortality data. Note the dramatic difference in ranges. Also, the NLR biomarker is calculated and does not have a reference range. Dividing two numbers is beyond the grasp of health authorities. This is plausible because creating good health is beyond the grasp of these same authorities.

Revolutionary Marker	Standard of Care Range	Science-based Reference Range
Insulin	2.6 – 24.9 uIU/mL	1.5 – 4.0 uIU/mL
NLR	Not Determined	0.6 – 1.5
ESR	0 – 40	0 - 2

Table 4.1. Important biomarkers and their reference ranges.

Good health does not have to be expensive. When you see your doctor, the blood drawn is the same every time, regardless of your health status or complaints. The total cost for these labs is relatively low. Provided in Table 4.2 is an estimate of

their charges. These are safe labs for your doctor to draw. If any of the biomarkers in the panel are elevated, they have a drug to give you to relieve them of any liability associated with inaction. Most doctors are unfamiliar with interpreting the revolutionary markers and what to do to improve them.

Standard of Care Biomarkers	Cost	Revolutionary Biomarkers	Cost
Metabolic Panel	\$2.25	Fasting Insulin	\$3.00
Cholesterol	\$3.00	NLR	\$1.80
CBC	\$1.90	ESR	2.00
Total	\$7.15	Total	\$6.80

Table 4.2. The costs of typical standard-of-care biomarkers and the cost of revolutionary biomarkers.

Too many of us assume we are healthy. After all, we have not been to the hospital or had surgery. However, many people have nagging health complaints that do not constitute a diagnosable disease, so the minor irritation simply festers. Moreover, the problem might not be continuous and just erupts occasionally. People with these health issues fall into an expansive group called the “apparently well.”

Being apparently well is dangerous because many chronic diseases strike without notice, and there can be a long incubation period before a big adverse event. The person received warning signs – nagging low-grade health problems. Normal labs based on the outrageously inaccurate standard of care reference ranges almost always indicate no detectable health issue. Sometimes we are told the problem is “all in our head.” Then, you suddenly realize, too late, that it was not just in your head. Soon after, you begin to understand health is not in your doctor's head.

The current sick care system, which needs a revolutionary change, assumes you are either healthy or ill, and there is no ground in between. This is, our course, intuitively incorrect. For example, a person who just suffered a massive heart attack was not perfectly healthy the minute before, the hour, day, week, month, year, or decade before that unfortunate event. They might have thought they were or been told so by their doctor.

The simple but revolutionary truth is that we all live on a health-disease continuum. And knowing your location on that continuum and what you can do to improve your position is the transformational change we all need to achieve healthy longevity. However, to understand your health, the labs drawn must encompass major categories of diseases while explaining processes that cause the diseases.

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The standard of care ICD-10 diagnostic book lists ~70,000 codes. With that vast number of diagnoses, educating people on health is next to impossible. How many biomarkers are required to understand your risk for a portion of 70,000 diseases? My guess is a shade more than the three discussed in this chapter! However, these codes are all “human-made” and reflect symptoms rather than underlying processes that drive disease.

The coding system is primarily about financial reimbursement and managing what a doctor can and cannot do. For a medical provider to receive payment for medical services, ICD-10-CM codes must be submitted to the payer. While CPT® codes depict the services provided to the patient, ICD-10-CM codes depict the patient’s diagnoses that justify the services rendered as medically necessary. Prevention, although becoming a more popular term, barely fits into the ICD-10 and CPT® coding systems and is infrequently used. However, with the revolutionary approach, applying the health-disease continuum concept, prevention is not a concept. Instead, the objective is to optimize health regardless of our human-defined health status. Therefore, the word “prevention” does not occur in "optimization."

In so many cases, we are given meaningless diagnostic codes. The person with the disease knows they have a health problem, in most cases, but the diagnostic codes are often so vague they provide no insight into why or what to do. The person is usually offered one of three things: 1. nothing, 2. a prescription, or 3. surgery. For example, consider multiple sclerosis (M.S.) coded in the 2022 ICD-10-CM Diagnosis Code as G35. The word “multiple” means “many,” and the term “sclerosis” means “abnormal hardening of body tissue.” Not a very helpful diagnosis, and the standard of care offers no bonafide treatments.

A person with M.S. knows they are destined for a slow and miserable decay of neurological and whole-body function. Yet, some doctors have properly diagnosed and reversed this condition. Sadly, this is a very rare happenstance because those diagnostics and treatments are not in the ICD-10 code book, so most people are, and will continue to be, underdiagnosed and treated.

Chronic vs. Acute Health

Revolutionary change is a move to an objective and science-based system instead of the subjective symptoms and population-based approach in which we are stuck. This change also involves separating health and healthcare delivery into acute and chronic categories. The standard of care is just an acute care system. At times, it is very good at managing acute health situations. However, the track record for chronic diseases in the United States and globally is abysmal. Therefore, the proposed revolutionary healthcare change has little to do with the acute care system and instead focuses entirely on chronic health. This segment constitutes 90 percent of healthcare expenditures and human misery.

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The revolutionary chronic disease system is based on disease mechanisms rather than symptoms. Five (5) key mechanisms drive most chronic diseases. They are:

1. Poor repair and recovery caused by low nutrient intake or poor digestion;
2. Chronic and often stealth infections;
3. Survive vs. thrive induced by stressors. This mechanism is often referred to as "fight or flight."
4. Chronic inflammation not caused by infections;
5. Lack of autophagy from constantly eating or inactivity.

These categories, at first glance, may appear vague and not particularly actionable. However, each mechanism is, in fact, easily measurable – particularly with the biomarkers in Table 4.1. Significantly, protocols for improving these mechanisms are readily available and effective. There are clear-cut solutions when understanding that one or more of these mechanisms are in play. If you have an M.S. syndrome, wouldn't you like to know some, or all, of the causes? That knowledge is empowering, often leading to actions. These mechanisms often have solutions that can be implemented on your own or with the help of a healthcare practitioner. But, that individual must know the concept of disease mechanisms and associated root causes.

Although applied in functional and integrative medicine, this chronic disease approach is not widely available because it does not have ICD-10 billing codes. This is the crux of traditional healthcare – if there is no billable code, no testing or interventions are obtainable - period. There are merits to controlling costs in many industries, but when it comes to your health, is it really appropriate to assign a price? More importantly, poor health is costly to both the patient and society long-term. Thus, a revolutionary proactive approach will save money near and long term.

Suppose doctors are given the freedom to provide solutions based on root causes and mechanisms, even if the initial costs are higher. In that case, there is an excellent likelihood that overall costs over the individual's life will be substantially lowered. The average healthcare cost for an M.S. sufferer is \$4 million.¹⁶⁰ According to Optum,¹⁶¹

“In addition to the spending for M.S. drugs, M.S. patients also have considerably higher overall health care costs than average. One reason is that M.S. patients often have additional medical conditions. These include physical conditions like fibromyalgia, inflammatory bowel disease, and epilepsy, plus psychiatric comorbidities like depression and bipolar disorder. With an estimated lifetime cost per M.S. patient of over \$4 million, M.S. is the second-ranked chronic condition (behind congestive heart failure) in direct all-cause medical costs. For the U.S., the total estimated cost of M.S. is \$28 billion per year.”

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When complex diseases like M.S. do not have a solution, the victim descends into a plethora of degenerative diseases. In these cases, costs multiply exponentially as doctors use expensive coded tools to manage escalating symptoms. Are there solutions to such conditions, however? If healthcare providers just deliver services based on ICD-10 and CPT codes – that is, doing the same thing repeatedly with no hope of improved health, the odds are low for finding a solution. M.S. is not an outlier, either. Major diseases like heart disease, Alzheimer’s, and cancer fit into this M.S. paradigm. That’s why our healthcare budget exceeds \$4,000,000,000,000 (\$4 trillion) annually.

David Wheldon, MD of the United Kingdom, and Charles Stratton, MD from Vanderbilt University have solved and, to a significant degree, reversed a few cases of MS.¹⁶² This does not mean that all M.S. patients can realize these results. However, learning occurs from success and failure. Moreover, failures often provide insights into mechanisms targeted by the failed approach. Sadly, medicine considers such results as “anecdotal” and not driven by evidence, so decades or more will pass before such approaches are accepted and adopted.

In the meantime, costs and misery add up. The price to reverse M.S., using the methods of Dr. Wheldon, is in the range of \$4,000. Let us do the math:

$$\$4,000,000 \text{ divided by } \$4,000 = 1,000.$$

That is, the standard of care approach is 1,000 times more expensive than Dr. Wheldon’s.

And the standard of care provides no relief from the disease. The potential savings for a single patient with M.S. over the life of the disease is

\$3,996,000.

Fundamental and inexpensive lab testing is available for everyone. The three tests covered in this chapter have the potential to bring initial clarity to the drivers of M.S. Dr. Wheldon did not run lipid panels, but he did tests for inflammation. But unfortunately, the standard of care testing for lipids, A1C, and chemistry is inadequate to start a healing approach for M.S. or most chronic diseases. There is a better way.

The proper testing for everyone involves assessing the five disease mechanisms. These mechanisms are initiated by a broad array of causes that are well-known and modifiable. Moreover, many biomarkers have the accuracy and precision to show that one or more of these mechanisms are in play. The three biomarkers in Table 4.1 stand out as particularly informative about chronic disease mechanisms and associated impactful interventions.

Fasting Insulin – A Marker of Malnutrition

Malnutrition, or a deficiency in nutrients, is the most important driver of chronic disease mechanism 1 – poor repair and recovery. Most people think malnutrition

is a third-world problem impacting a small set of impoverished people in the United States. Sadly, this is wrong. We have an epidemic of malnutrition in the United States, but most people are unaware that they are so afflicted. In the United States, at least with calorie intake, we are well-fed, mainly through low-value carbohydrate consumption. However, nutrition covers a much broader scope beyond calories. A definition of nutrition is “the process of providing or obtaining the food necessary for health and growth or the sum of the processes by which an animal or plant takes in and utilizes food substances.”¹⁶³ Note that the word “calorie” is not included in that definition.

Most of us believe that hunger results from a need for calories. But most Americans have plenty of stored calories surrounding their midsection and the rest of their bodies. Therefore, when searching with the usual engines for what causes the hunger response, you will mostly find answers that address a deficiency in calories. Thus, this is what we have been programmed to believe.

The website Healthline provides what is usually found when searching for hunger. In an article titled “14 Reasons Why You’re Always Hungry,” the author, Jerlyn Jones, states: “In the United States and other high-income countries, hunger is mainly caused by poverty that results from a lack of jobs or because jobs pay too little. Hunger rates rise when the national or local economy is in a slump. People lose jobs and cannot find work.”¹⁶⁴ The inference is a lack of food, thus calories, not a lack of nutrition. The hunger response, therefore, is only due to a lack of foodstuffs only.

Healthline states, “In the United States, 36.5 percent of adults have obesity. Another 32.5 percent of American adults are overweight. In all, more than two-thirds of adults in the United States are overweight or have obesity.” WebMD also makes a feeble attempt at explaining hunger, and the list they compile misses the point.¹⁶⁵ Below is a composite index of hunger drivers from Healthline and WebMD. Neither mentions a lack of food and nutrients. They belong on the list. This type of reporting is highly insensitive to the 38 million people in this country, including 12 million children who are food insecure.

- Diabetes
- Low blood sugar
- Lack of sleep
- Stress
- Diet
- Medications
- Pregnancy
- Thyroid problems
- Diet soda
- Dehydration
- Too much exercise

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- Insufficient protein
- Too many refined carbs
- Low-fat diet
- Low fiber intake
- Eating while distracted
- Too much alcohol
- Drink your calories
- Eat too fast
- Medical conditions

When food is available, the actual cause of hunger is one simple thing – a nutritional deficiency of any kind. These include insufficient macronutrients – carbohydrates, proteins, fats – and, more importantly, micronutrients. Micronutrients drive repair and recovery processes being the activating components of enzymes. The article “The Central Role of Enzymes as Biological Catalysts”¹⁶⁶ explains that “Enzymes accelerate the rates of biological reactions by well over a million-fold, so reactions that would take years in the absence of these catalysts can occur in fractions of seconds if catalyzed by the appropriate enzyme. In many cases, metal ions (such as zinc or iron) are bound to enzymes and play central roles in the catalytic process.”

The search has to be very targeted to get the correct answer about what drives hunger. This is because there is substantial bias in the results of most internet searches on this topic. For example, searching “what makes you hungry” leads to the list below. To find the correct answer, you must already know what it is, making the search engines useless.

Rick Tague, MD, provides much better insight into hunger than popular sites. In his article, “3 Ways Vitamin Deficiencies Cause Weight Gain,” Dr. Tague gets right to the point.¹⁶⁷ He states:

“Reason #1 – Cravings

Low nutrient levels in the brain's appetite center can trigger a ravenous appetite and uncontrollable cravings! Our brain's appetite center has receptors that know if we are deficient in crucial nutrients like iron, vitamin D, or B vitamins. If we are deficient, our appetite center gets turned on, and we will eat more. Often the cravings are excessive, relentless, and irresistible, especially for tasty, high-calorie foods that cause excessive weight gain.

Reason #2 – Fatigue

Low nutrient levels cause fatigue, limiting activity. When we are tired, we are less active. Chores, shopping, and fitness activities just don't get done! This fatigue, often due to missing key nutrients, will sabotage the best intentions to be fit and active. More unwanted weight gain occurs from less activity.

Reason #3 – Slow Metabolism

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Missing nutrients slows the metabolism. Essential nutrients play key roles in our body chemistry. Nutrients build muscle and bone, create energy, burn sugar and fat, and keep mood regular. A slow metabolism will also contribute to progressive unwanted weight gain if you aren't getting all your vitamins and minerals.

Conclusion: Nutrient deficiencies WILL lead to unwanted, progressive weight gain!”

A German nutritionist Hans K. Biesalski is a world expert on “hidden hunger.” His work illuminates a global problem due to inadequate intake of vital micronutrients.¹⁶⁸ It is a problem in the rich world but a bigger one for the poor. In his opinion, billions of people suffer from this kind of hunger that may or may not manifest as a hunger response. However, the effects of chronic insufficient micronutrient intake are chronic diseases.

According to Biesalski, “chronic undernutrition is often overlooked because it takes a long time for it to manifest itself as illness. But the effects can be devastating. Children suffer from impaired physical and mental development and face a mortality rate many times higher than children with a healthy diet. In adults, the immune system can be weakened, and in pregnant women specifically, deficiencies of micronutrients such as iron result in higher perinatal mortality.”

With no food insecurity, many Americans eat on a three-meal-a-day routine and never experience hunger. In essence, they are circumventing the hunger response. However, it does not mean they are not malnourished. The act of eating simply quells that response. Your brain, your master regulator of all processes, hopes the latest intake satisfies a deficiency and needs to wait for the food to be processed before passing judgment.

We can measure malnutrition in populations with one fundamental and low-cost test – fasting insulin.

Fasting insulin has a couple of key companion markers, ghrelin, and leptin, for which tests are available. However, fasting insulin is more than adequate as a screening tool for malnutrition. Including these additional tests improves precision, but they are substantially more expensive than the insulin test. In addition, a plethora of tests for nutrients such as iodine, magnesium, iron, B vitamins, selenium, amino acids, and electrolytes add insight into malnutrition and hunger.

Fasting insulin testing is used mainly as a marker of diabetes. In the standard of care, diabetes testing seldom includes fasting insulin, though, and instead, HgA1C and fasting glucose levels are used. This approach provides further insight into the lack of precision and potential ignorance of traditional doctors. Diabetes is a human-made term for profound insulin resistance. There is no actual line of demarcation between a diabetic and a non-diabetic – everyone lies somewhere on the metabolic continuum. Instead, the assignment of a diagnosis is more for convenience, coding, and prescription writing than for science.

Fasting insulin is at the root of disease because micronutrients play a critical role in tissue and cellular rebuilding, repair, and recovery. Importantly, fasting insulin is the most sensitive of the metabolic barometers. Insulin is a peptide hormone produced by beta cells of the pancreatic islets; it is considered the body's primary anabolic (building tissue and storing energy) hormone. It regulates the metabolism of carbohydrates, fats, and protein by promoting glucose absorption from the blood into the liver, fat, and skeletal muscle cells. In this regard, glucose, HbA1C, and triglycerides are subordinate to insulin.

Since insulin is regulatory, and the other metabolic substances respond to the action of insulin, the process of developing insulin resistance and eventually being classified with diabetes typically follows this course:

- First, excess calories – particularly in the form of carbohydrates are consumed.
- Insulin responds and “pushes” the glucose out of the blood into cells.
- As this process continues, insulin levels elevate, but glucose and A1C stay relatively normal.

Perpetuation of this process causes insulin to be overwhelmed (its level goes quite high), and glucose levels start to rise. Note – glucose elevation lags behind that of insulin.

HbA1C is a red blood cell with a glucose molecule attached and is properly called glycosylated hemoglobin. All red blood cells are replaced every four months. As glucose levels in the blood increase, so does the concentration of this glucose-blood cell complex. However, the increase in HbA1C concentration lags behind that of glucose because it is an average over four months. In most cases, glucose was lower four months ago than today based on trends in diabetes in our society.

Eventually, as insulin is tapped out (profound insulin resistance) glucose, then A1C rise to above normal values similar to that of insulin.

In many instances, a person with “tapped-out” insulin is put on insulin therapy, which exacerbates insulin resistance even if glucose and A1C levels decrease slightly.

Thus, insulin is a more forward-looking marker than glucose, and A1C is the most backward-looking of the three biomarkers.

The steps to reversing the insulin resistance process are the reverse of what created the resistance. Again, an actual clinical case is illustrative. Ed was on insulin, metformin, statin, and a blood pressure medication when he became a participant in a wellness program. Interestingly, he indicated that his blood pressure was never really elevated, yet he still walked away from a clinical visit with a prescription. Through dietary changes, including lowering carbohydrates and increasing micronutrient intake, Ed could discontinue insulin. As he continued this improved diet over a series of months, his insulin levels slowly

decreased from the 60s to the teens. At month six, his fasting insulin was 14, his fasting glucose was down from 320 to 150, and his A1C went up from 7.8 to 8.2. A1C, at this point, reflected his glucose months before – as explained above.

Ed had a routine doctor visit after making great strides in reducing his “diabetes” status. The doctor, however, showed a complete lack of understanding of the diabetes process and put him back on insulin and increased his metformin. Like many in the standard of care, this doctor used A1C to determine therapy without considering the fasting insulin level, which clearly showed an improvement in his metabolic state. Ed worked very hard to improve his metabolic status and was decidedly discouraged by his doctor’s action. Ed fired the doctor, replaced metformin with berberine, and today is medication free, including eliminating blood pressure medication and the statin, which is well known to make diabetes worse.¹⁶⁹

Different schools of thought regarding insulin resistance's mechanism(s) exist. The key ones are:

1. a reduced concentration of insulin receptors on cells;
2. reduced concentration of insulin-regulated glucose transporters; and
3. Attenuation of positive feedback to the insulin receptor substrate; and glucose overflow, all of which come under the umbrella of “internal starvation.”

Dr. Jason Fung explains the “glucose overflow” mechanism in his article titled “The Biochemistry of Insulin Resistance”¹⁷⁰ as follows.

“A cell can hold only so much ATP (energy). Once these stores are full, they cannot hold anymore. The logical action is to stop putting more “gas” (glucose) in the tank. This means that the cell must stop the inflow of nutrients into the cell. When there is too much ATP, the ATP itself and some of the intermediates act upon the entire process to slow it down. When you are pumping gas into your gas tank, and the tank gets full, the pump will automatically stop so that you don’t spill gasoline everywhere. The cell does the same thing.

Our exquisite metabolic system ensures that ATP is produced when needed but never in excess. When this process grinds to a halt, glucose at the top of the chain backs up. This slows down the production of ATP and restores the system to normal. But what if we keep feeding glucose into the system? As glucose increases within the cells, there is less and less of a concentration gradient for glucose to flow from outside to inside the cell. Hence, you see the glucose increasing in the blood outside, and hence the term ‘insulin resistance.’ But this is not a lock-and-key problem. It’s an overflow situation. As the term is commonly used, the underlying problem of ‘insulin resistance’ comes down to two simple things – too much glucose, which leads to too much insulin.”

Dr. Fung makes other important points:

- Excess glucose will be converted to fat by the liver
- The fat is moved by very low-density lipoprotein (VLDL), leading to high triglycerides and low HDL.
- Dietary fat and carbohydrates are mainly useful as sources of energy.
- Excess proteins are converted to sugar by the process of gluconeogenesis. However, there is no storage container for excess protein, so the body converts it to sugars, then stores it as fat.
- Insulin resistance, while carbohydrate dominated, can also be activated through, for example, too much fat (triglycerides) or protein. In addition, any macronutrient may produce ATP, which will overload the system and cause glucose to back up. The logical solution? Fasting and exercise.

The American Diabetes Association (ADA) has a different view of insulin resistance than Dr. Fung, as explained in the article “Understanding Insulin Resistance.”¹⁷¹ According to the ADA, “Insulin resistance is a hallmark of prediabetes and type 2 diabetes.” It says, “People with insulin resistance, also known as impaired insulin sensitivity, have built up a tolerance to insulin, making the hormone less effective. As a result, more insulin is needed to persuade fat and muscle cells to take up glucose and the liver to continue to store it. Why a person fails to respond properly to insulin is still a mystery.” However, it does indicate that insulin levels are associated with the disease and its severity. Maybe Dr. Fung explains that mystery, as stated above.

Inflammation also plays a role in insulin resistance. Inflammation is a generic term for an immune response to an insult affecting the body that is either infectious or irritating. Over the past decades, obesity has been recognized as a disease of inflammation. The article “Metabolic inflammation and Insulin Resistance in Obesity”¹⁷² was published in the prestigious journal *Circulation* in 2020. The summary reproduced below explains the interplay between insulin resistance and inflammation.

“Most studies still support that inflammation plays a causal role in developing insulin resistance. Alternatively, inflammation may play differential roles in different conditions or stages of obesity. Once initiated, inflammation and insulin resistance may exacerbate each other. For example, adipose tissue inflammation may contribute to local and systemic insulin resistance through autocrine (signaling) effects of inflammatory cells or molecules on insulin signaling and metabolism in adipocytes (fat storage cells) and endocrine effects of inflammatory molecules secreted by fat cells (known as adipokines) on insulin sensitivity in other tissues, particularly skeletal muscle and liver. In addition, adverse effects of inflammation on preadipocyte/adipocyte metabolism can accelerate fat spillover from adipose tissue to skeletal muscle and liver, resulting in

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unexpected fat deposition and insulin resistance in these tissues, which play vital roles in systemic insulin resistance and type 2 diabetes.”

It is important to understand what causes insulin resistance and how this relates to malnutrition. You will find few in the medical profession that associate fasting insulin with malnutrition. Regardless, fasting insulin is the central measure for metabolic dysfunction, which is caused by malnutrition in many cases.

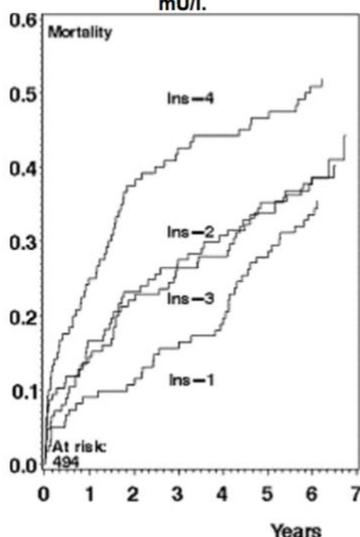
The logic that the fasting insulin value is a measure of micronutrient malnutrition is straightforward.

A lack of calories drives hunger. Only a minority of people in the developed world lack adequate caloric intake. Also, “silent hunger,” or a deficiency in micronutrients, causes a hunger response. People with silent hunger include a substantial population in the developed and undeveloped world. Here is the sequence:

- An individual starts with complete insulin sensitivity – metabolically, he or she is in homeostasis.
- The Standard American Diet (SAD) or equivalent high carbohydrate diet with processed foods, which are both low in micronutrients, is consumed.
- The consumption of calories is more than required, and the excess is stored in the body as fat, but low-value food causes a micronutrient deficiency and silent hunger, driving the desire for more food.
- As low-value food is constantly consumed, silent hunger perpetuates. If not curbed, this process leads to a downward spiral into insulin resistance, weight gain, obesity, and an eventual diagnosis of diabetes.

Fasting insulin is a valuable biomarker because it is a barometer for malnutrition and early mortality risk. The two, of course, are related. Malnutrition is somewhat complicated to measure, whereas data on the relationship between fasting insulin and premature mortality statistics are readily available in peer-reviewed journal articles. A strong relationship exists between fasting insulin and all-cause mortality. Figure 5.1 shows the risk, which rises rapidly for Insulin levels above 6.4 mU/l.¹⁷³ Mortality data below six (<6) is not easy to find and may be confounded by type 1 diabetes in some instances, but the absolute optimal insulin level is between 1.5 and 4 mU/l.

Cumulative mortality from all causes stratified in quartiles of fasting plasma insulin: First: insulin <6.4 mU/l; Second: insulin 6.4–9.3 mU/l; Third: insulin 9.4–13.5 mU/l; Fourth: insulin >13.5 mU/l.



Charlotte Kragelund et al. *Eur Heart J* 2004;25:1891-1897

Figure 5.1. Cumulative mortality from all causes stratified in quartiles of fasting plasma insulin: First: insulin <6.4 mU/l; Second: insulin 6.4–9.3 mU/l; Third: insulin 9.4–13.5 mU/l; Fourth: insulin >13.5 mU/l.

Risk expressed by many biomarkers follows a “U” curve. When a biomarker or vital sign is too low, the risk of dying prematurely increases. For a biomarker elevated above normal, this is also the case. Insulin is no exception. According to Lee,¹⁷⁴ “Both type 1 and type 2 diabetes are well-established risk factors for cardiovascular death and early all-cause mortality. People with type 1 diabetes (T1D) have a three- to four-fold increased risk of premature death compared with the general population. T1D is also associated with an increased risk of cardiovascular disease (CVD), including myocardial infarction (MI), heart failure (H.F.), and atrial fibrillation (A.F.). Low serum insulin level is associated with all-cause mortality and cardiovascular mortality in acutely decompensated heart failure patients without diabetes mellitus.”

In COVID-19, insulin resistance and supplemental insulin correlated to a higher risk of death than those who did not use insulin. The increase in mortality reported was severe, 260 percent higher compared to people not on exogenous insulin therapy.^{175, 176} Importantly, in this study, the people on insulin therapy and those who were insulin sensitive were not compared. Instead, they were compared to those just not on insulin. In other words, they were compared to people, many of whom had insulin resistance. Therefore, compared to insulin-sensitive people, the mortality risk is much higher than 260 percent.

Diabetes, thus insulin resistance, shows a strong association with an increased risk of early mortality in infectious diseases. Importantly, this risk is not just

associated with the SARS-CoV-2 virus. Diabetes and high fasting insulin are significant predictors of the severity and death of patients infected with viruses, including Middle East Respiratory Syndrome (MERS).¹⁷⁷ The mechanism is straightforward. Insulin resistance promotes inflammation and end-glycosylation products, including elevation in HbA1C, resulting in a higher likelihood of infection and a worse prognosis. The infection leads to the destruction of pancreatic beta cells that release insulin and results in higher levels of glucose and more significant swings in glucose levels in the blood. In this respect, fasting glucose, insulin, and HbA1C levels clearly represent mortality risk. Malnutrition, associated with insulin resistance, is a leading factor in the mortality risk.

Be cautious about using pharmaceuticals to regulate glucose levels to reduce mortality risk, especially when viral infections are present. A little-known, but important study, is called the ACCORD trial.¹⁷⁸ ACCORD is an acronym for “Action to Control Cardiovascular Risk in Diabetes.” A clear conclusion from this study is that “tight” control of glucose levels using drugs leads to much worse outcomes. When glucose elevates (often insulin levels are not tested), many doctors prescribe drugs, including insulin and metformin, to bring glucose levels down. Often their goal is to achieve glucose levels seen in insulin-sensitive people, less than 100 mg/dL.

The outcomes during the ACCORD study were so bad, with mortality increasing significantly within a short period of time the researchers stopped the study. Stopping a study is a highly unusual event in clinical trials and shows the adverse impact of trying to override what our body is naturally trying to do. In this case, highly insulin-resistant people need excess glucose to overcome insulin resistance and supply cells with fuel.

In a statement from the American Diabetes Association (ADA), “The ACCORD study terminated its glycemic control study early due to the finding of increased mortality in participants randomized to a strategy of very intensive glycemic control with a target A1C of 6 percent. The findings of these three major trials led the ADA, with representatives of the American Heart Association (AHA) and the American College of Cardiology (ACC), to reexamine the recommendations for glycemic targets in patients with diabetes, the majority of whom have type 2 diabetes.”¹⁷⁹

Caution: Many doctors may not know they can “overcontrol” blood sugar levels. However, if this happens, signs and symptoms of hypoglycemia will become evident, even if your blood sugar is still above “normal” values. Seek medical advice.

Neutrophil to Lymphocyte Ratio – Marker of Infection

What is the Neutrophil to Lymphocyte Ratio (NLR)? It is the ratio of your absolute neutrophils divided by absolute lymphocytes. The NLR obtains from a complete blood count with a differential test that costs less than \$2. Note this test

also provides neutrophil and lymphocyte percentages. These values do NOT yield the NLR.

Doctors rarely calculate the NLR. Instead, they quickly glance at the total white blood cell counts and almost always conclude, “they are fine.” But, of course, they do not understand that the standard of care reference ranges is too broad, so the WBC values are not acceptable in many cases. Instead, the value is an indication of smoldering risk. Additionally, the NLR itself does not have a reference range. Without a reference range, a traditional doctor is ill-equipped to draw conclusions about the association of its value to risk.

The medical research community is well-apprised of the prognostic value of the NLR. Web searches using the term “neutrophil to lymphocyte ratio” returns 9,000,000 articles. Using the same phrase, a more targeted search within the National Library of Medicine yields 35,000 articles. The NLR value titrates to many of the devastating human-defined diseases.

- NLR and Cancer: 28,000 articles
- NLR and Heart: 16,000 articles
- NLR and Cardiovascular: 21,000 articles
- NLR and Stroke: 6,500 articles
- NLR and Diabetes: 15,000 articles
- NLR and Infection: 21,000 articles
- NLR and Mortality: 24,000 articles

This search type does not necessarily demonstrate causation but illustrates a strong association between these disease syndromes and the NLR value.

Chapter 3, on immunity, describes the purpose of neutrophils and lymphocytes. Neutrophils are the effector cells in the innate arm of the immune system. They constantly patrol the host for signs of microbial infections, and when found, these cells quickly respond to trap and kill the invading pathogens. The key term is “microbial infections,” and neutrophils usually react to bacterial infections. Lymphocytes circulate in mammalian blood and are part of the innate immune system. There are two main types of lymphocytes: T cells and B cells. B cells produce antibody molecules that can latch on and destroy invading viruses or bacteria. T cells are part of the immune system and develop from stem cells in the bone marrow. They help protect the body from mainly viral infections and might help fight cancer, as viruses induce many cancers.

The NLR is not always a perfect marker for infection because, in some instances, neutrophils might go down, and lymphocytes might go up when an array of infectious species attacks the body. However, the NLR marker always comes with a complete white blood count with a differential that includes 18 individual biomarkers. Therefore, a doctor skilled at interpreting labs can use other white

blood cell counts to draw conclusions or diagnose. These biomarkers include neutrophil percent, total white blood cell counts, red blood cell distribution width, monocyte, eosinophil, and monocyte counts.

The NLR marker's high sensitivity is more informative than single white blood cell values. The ratio of the NLR amplifies both values. The NLR may elevate when the neutrophil and lymphocyte values are normal. The NLR amplifies the white blood cell count signal. In this case, “elevated” means the level of the NLR is associated with higher mortality risk based on published studies.¹⁸⁰

Harvard Medical School at Dana Faber Cancer Research understands the value of the NLR as a prognostic indicator of solid tumor cancer risk and outcomes. Aly-Khan Lalani, MD, is an Assistant Professor at McMaster University and a Medical Oncologist at the Juravinski Cancer Centre. After completing Internal Medicine and Medical Oncology training, he was awarded the T.D. Insurance Meloche Monnex & Alberta Medical Association Scholarship. After that, he pursued a Fellowship in Genitourinary Oncology at Dana-Farber Cancer Institute in Boston, mentored by Dr. Toni Choueiri. He has also completed the Program in Clinical Effectiveness at the Harvard T.H. Chan School of Public Health. He remains a Visiting Scientist at Dana-Farber and is a member of the Escarpment Cancer Research Institute, with academic interests in clinical trial design and translational work. In two separate interviews, Dr. Lalani stated:

Interview 1:

“We examined the ratio of the neutrophils to lymphocytes in metastatic Renal Cell Carcinoma (RCC) patients treated with immunotherapy. First, for some background, we know neutrophils reflect cancer patients' inflammatory cascade. We know that lymphocytes are an important anti-tumor agent, a suppressor of tumor growth pathways.

When we have this ratio of neutrophils to lymphocytes, we try to understand both the inflammation cascade and the immunotherapy response. The NLR, as we call it, has been studied in various solid tumors and has shown that it is associated with poorer outcomes in patients with higher NLR.

What has not been studied is looking at metastatic RCC patients, specifically in this expanding era of immune checkpoint blockade (biologic drugs). As we know, there is approval for nivolumab as the second-line agent, and the clinical trials ongoing with immunotherapy are expanding in RCC coding. So this is the perfect time to examine this kind of blood biomarker that is readily available, affordable, and modifiable in these solid tumor patients.”

Interview 2:

“In our study, what I find interesting and the major take-home point is, at the 6-week mark (of therapy), higher NLR was associated with worse objective response rate as well as poorer or shorter PFS (progression-free survival) and O.S. (overall survival) compared to those with lower NLR. I think that is very informative for physicians and patients. However, we also found that in those patients – when comparing baseline to the six-week level – patients that had a decrease in their NLR by 25% or more actually portended a more favorable outcome in terms of progression-free and overall survival compared to patients who had an increase in their NLR by 25% or more.”

Note that Dr. Lalani is a “scientist,” not a doctor. Thus, he is doing research and not applying his knowledge clinically. How is Harvard Medical School, at their oncology arm, Dana Faber Cancer Institute, applying this knowledge clinically? If you are a cancer patient, has a doctor told you your NLR and what you can do about it? The answer is probably >99.9 percent that your doctors did not tell you about this marker. Here is a real-life example of how little new knowledge is translated from the research side of medicine to the clinical application side.

Jim is a very dear friend. He has had metastatic cancer of the lungs for several years and is a patient at Dana Faber. I happened to be in Boston and gave Jim a call. He indicated he, too, was in Boston for a checkup with his Oncologist at Dana Faber. So, I went to Dana Faber and met him in the waiting room before his checkup. I asked if I could be invited to the consult, and, through some miracle, I was invited to listen – and I did, quietly for 30 minutes. At the end, I decided to ask one simple question, “what is Jim’s vitamin D level?” The oncologist quickly replied that they take vitamin D levels routinely. So, I asked the question again – what is his (pointing to Jim) level of vitamin D? The doctor claimed he did not have it in the chart with him.

The next day, Jim called me and said that after I left, they pulled blood on him, and his vitamin D level was 9ng/ml, whereas 55 – 80ng/mL is optimal for health and cancer prevention. The Dana Faber Oncologist blatantly lied about obtaining vitamin D levels on Jim, who has been a patient for several years. Clearly, there is a disconnect between medical research at Harvard and clinical delivery. Dana Faber’s research group has published prolifically on the benefit of high doses of vitamin D and cancer, yet it is not an intervention used by their oncologists.¹⁸¹ Thus, you can guess that the NLR marker receives even less consideration than vitamin D in clinical oncology.

NLR and Early Mortality

The connection between elevated NLR values and early mortality is not new knowledge. Peer-reviewed papers on this go back to the 1980s, but the studies were on animals. It took another 20 years for study reports on humans with this marker to appear. The first paper, titled “Which White Blood Cell Subtypes Predict Increased Cardiovascular Risk?”¹⁸² reports on various white blood cells

and indicate that NLR is most predictive. According to this research, “Total WBC count is confirmed to be an independent predictor of death and heart attacks in patients with or at high risk for coronary artery disease (CAD), but high Neutrophils or low Lymphocyte counts provide the greater predictive ability. The NLR value affords the greatest risk prediction. The NLR explored post hoc proved to be the most powerful single WBC count predictor, with a value of 5 or more elevating risk by 300% compared to ratios <2.”

More current research illustrates the predictive power of the NLR value in early mortality. For example, in a paper titled “The neutrophil-to-lymphocyte ratio is associated with mortality in the general population: The Rotterdam Study,” an NLR value of approximately 1.5 or less is shown to be optimal.¹⁸³ The Rotterdam Study, a long-standing, population-based, prospective cohort study of an aging population, was well respected and started in 2002. Figure 5.2 shows mortality trends with different NLR values over time.

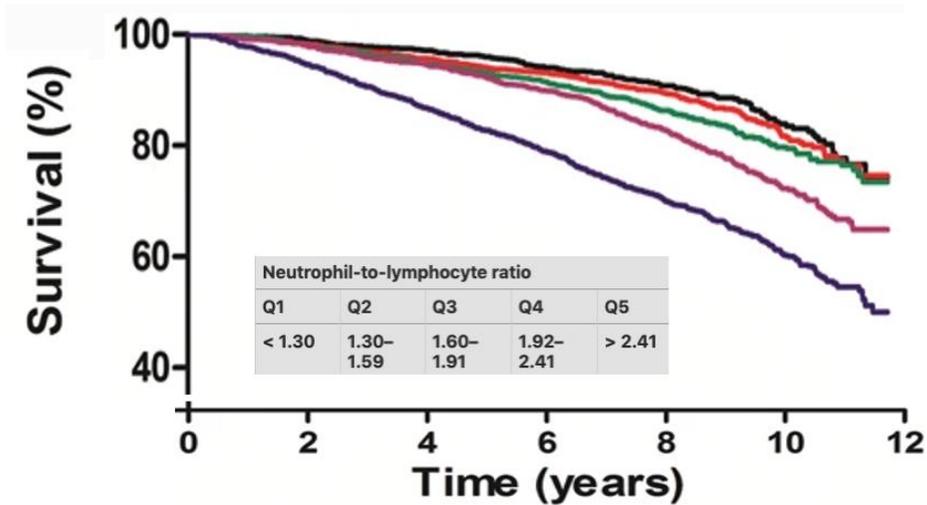


Figure 5.2: Kaplan–Meier (statistical) curves for all-cause mortality for each quintile of the NLR (P-value < 0.001). The upper black line is for Q1, and the lower line is for Q5. Q2 – Q4 reflect progressively lower survival rates.

What is the approach to lower elevated NLR? Many of us know what to do to reverse insulin resistance, and if not, most functional or integrative doctors or a health coach can help improve your metabolic status without drugs. But the NLR is less well understood. The COVID-19 pandemic provided substantial education on and appreciation of infection. Sadly, the relentless focus on vaccination has ruined a great opportunity for all of us to understand how to lower our NLR values by reducing infection.

Acute infections and their consequences are well appreciated. People get sick, often with an elevated temperature, at which point antibiotics are often prescribed. If a cold strikes, there are no pharmaceutical treatments and many people take

vitamin C and zinc while waiting for the adaptive immune system to conquer the virus. But chronic infections are a completely different paradigm. Firstly, 99.9+ percent of doctors do not recognize chronic infections or consider them a cause of disease. Instead, the doctor may assign a diagnosis, and the CPT code determines your boilerplate treatment path for your symptoms. According to the standard of care, cancer with elevated NLR is unrelated to infection. In the interview from Dana Faber cited above, there is no mention of infection. Likewise, cardiovascular disease, strokes, high blood pressure, and heart attacks have no relationship to infection in the standard of care.

Consequently, patients are given statin drugs to lower LDL, blood pressure medication to lower blood pressure, and may get a stent to circumvent an arterial blockage. Each of these treatments is for symptoms. However, what is the NLR in these diseases? Based on research, it is most likely elevated and a strong indicator of an underlying chronic infection.

In this context, many organisms, called pathogens, cause either disease or “disease.” The severity of the disease depends upon immune health and the pathogen's virulence. Treatment of chronic infections is different compared to acute infectious diseases. Chronic infections, like chronic diseases, require long-term treatment to eradicate what is defined as “obligate intracellular pathogens.” These pathogens are different from those that cause acute infectious diseases like the flu because they can hide from treatment over long periods, thus requiring longer treatment approaches. In all cases of illness, the best approach is to improve immune health. The starting point is to evaluate and improve diet and digestion. Supplements are part of the immune health equation when quality whole foods are unavailable or routinely consumed. Anti-pathogenic nutrients include vitamins A and D and a variety of herbs. Finally, everyone can measure their progress in the fight against chronic infections and disease by obtaining the neutrophil to lymphocyte ratio through a complete blood count with differential.

Erythrocyte Sedimentation Rate – Marker of Electricity

A single biomarker never conveys a detailed story about health. However, if given just one biomarker, the erythrocyte sedimentation rate (sed rate, ESR) is arguably the most informative about health. This test is quite interesting. It measures how red blood cells (RBCs) in blood serum settle in one hour. An ESR value of 15 means red blood cells have settled 15 mm in a test tube in one hour. Healthy cells do not settle, meaning they defy the forces of gravity. Try dunking a basketball to appreciate the power of the gravitational pull. What is this force on red blood cells that defies gravity, and what does it infer about health? Notably, the ESR does not just explain forces on red blood cells. All cells in the human body are composed relatively the same way, with a phospholipid bilayer structure. Thus, the ESR explains forces on all cells.

The book “The Cell: A Molecular Approach. 2nd edition,”¹⁸⁴ explains the importance of cellular membranes:

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“The structure and function of cells are critically dependent on membranes, which not only separate the interior of the cell from its environment but also define the internal compartments of eukaryotic cells, including the nucleus and cytoplasmic organelles. The formation of biological membranes is based on the properties of lipids, and all cell membranes share a common structural organization: bilayers of phospholipids with associated proteins. These membrane proteins are responsible for many specialized functions; some act as receptors that allow the cell to respond to external signals, some are responsible for the selective transport of molecules across the membrane, and others participate in electron transport and oxidative phosphorylation. In addition, membrane proteins control the interactions between cells of multicellular organisms. The common structural organization of membranes thus underlies various biological processes and specialized membrane functions.”

Upon searching The National Library of Medicine (NLM) from 1900 to the present, a minuscule number of references provide information on the mechanism by which your red blood cells defy gravity. However, a key paper has the title “Erythrocyte Sedimentation Rate.”¹⁸⁵ Key teachings extracted from this paper are presented here.

“The ESR test measures the rate at which the red blood cells (RBCs), or erythrocytes, in a sample of whole blood, fall to the bottom of the Westergren tube. This process of "falling" is called sedimentation.”

“RBCs typically fall at a faster rate in people with inflammatory conditions such as infections, cancer, or autoimmune conditions. These conditions lead to an increase in the number of proteins in the blood. This increase causes red blood cells to stick together (clump) and settle at a faster rate. A group of RBCs that are clumped together will form a stack (similar to a stack of coins) called a Rouleau (plural is rouleaux). Rouleaux formation is possible because of the particular discoid shape of RBCs. The flat surfaces of the RBCs allow them to contact with other RBCs and stick together.”

Note: The article states that increases in inflammatory proteins cause the RBCs to stick together. This explanation does not adequately explain why the proteins cause this effect.

“Normally, RBCs have negative charges on the outside of the cells, which cause them to repel each other. Many plasma proteins have positive charges and can effectively neutralize the negative surface charges of the RBCs, which allows for the formation of the rouleaux. Therefore, an increase in plasma proteins (present in inflammatory conditions) will propagate an increase in rouleaux formations, which settle more readily than single red blood cells. The settling of the rouleaux aggregates in the Westergren tube occurs at a constant rate. The rouleaux formation allows the RBCs to settle

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at a faster rate, thus increasing the ESR. Therefore, the ESR is not the measure of a single marker but a physical process.”

Note: It is getting closer to the truth. The positively charged proteins neutralize the charge on the red blood cell's outer membrane. However, this does not address how the negative charges get on the cells in the first place.

“Rouleaux formation (and thus the ESR) is affected by the amounts of immunoglobulins and acute phase proteins (prothrombin, plasminogen, fibrinogen, C-reactive protein, alpha-1 antitrypsin, haptoglobin, complement proteins) that are present in several inflammatory conditions.”
"Acute-phase proteins" (APP) is the name given to a class of approximately 30 distinct, chemically unrelated plasma proteins that are innately regulated in response to infection and inflammation. APPs are produced by the liver and are functionally controlled by the body in response to several forms of tissue damage or insult. These proteins act as inhibitors or mediators of the inflammatory response.”

Note: What a deal! This fundamental and inexpensive test is an indicator for 30 different cytokine biomarkers. To run each of these tests individually would cost thousands of dollars.

“The detection of the first acute phase protein in the 1930s, the C-reactive protein (CRP), occurred during the analysis of the plasma of patients diagnosed with acute pneumococcal pneumonia. The CRP and many other acute-phase proteins may increase during ongoing tissue damage, either acutely or chronically. "Acute phase" is still used to label these proteins that change in concentration during certain disease processes, regardless of chronicity. The fluctuating nature of the acute phase proteins in inflammation leads to the increased "stickiness" of RBCs, the formation of RBC "stacks" (rouleaux formation), and an increase in ESR.”

Note: The term “acute phase” concept is very important in understanding health. Minor injury or an acute infection, one noticeable to you as opposed to a chronic infection, may temporarily raise cytokine levels, and the person will feel apparent symptoms, such as cold or flu. As an example of how APPs change with injury, a healthy participant in our wellness program retested his labs shortly after returning from vacation. His fibrinogen level was substantially higher than this test run four months previously, while all his other labs improved. Upon exploring this with him, he rolled down his sock and showed a large gash. He was camping and chopped himself rather than the piece of wood at which he was aiming. A whole week later, his fibrinogen, a signal molecule that tells the body there is an injury needing repair, was still elevated but probably much lower than right after the injury.

Fibrinogen can also rise chronically, whereas, in the example above, it is elevated in response to a sudden (acute) injury. The article “The multifaceted role of

fibrinogen in tissue injury and inflammation” explains acute versus chronic elevation of proteins indicative of an inflammatory process that can impact ESR levels.¹⁸⁶ “Fibrinogen and proteases (enzymes) controlling its deposition and clearance have powerful roles in driving acute and reparative inflammatory pathways that affect the spectrum of tissue injury, remodeling, and repair.”

Although many inflammatory illnesses will increase the ESR, other conditions exist that can lower the ESR. These “lowering factors” can exist either as isolated disease processes or in conjunction with other pathologic conditions that raise the ESR, thus giving a “lower than expected” ESR results in light of a severe underlying inflammatory process. For example, Polycythemia (an increased number of red blood cells) will increase blood viscosity and can cause a reduced ESR (reduces the rate at which RBC rouleaux will settle to the bottom of the Westergren tube).

Some blood diseases, although rare, such as sickle cell disease, can lower ESR due to the abnormal shape of red blood cells that impairs rouleaux formation. Spherocytosis (the presence of sphere-shaped rather than disc-shaped RBCs) also inhibits the rouleaux formation and can decrease the ESR. Multiple factors impact the values for most biomarkers. This is why a single test is never adequate at characterizing health. Instead, our doctors use a minimum of 20 biomarkers associated with chronic conditions. And, since all our biomarker “normal” values are tied to early all-cause mortality risk, we produce a single health score that is easy to understand and allows health tracking upon retaking the lab panel.

In the article “The Erythrocyte Sedimentation Rate: Old and New Clinical Applications,”¹⁸⁷ a group from Alabama weighed in on how ESR is an indicator of other cytokines in your blood.

“Cytokines are glycoproteins produced by different cells involved in the immune response. They enhance or regulate inflammation by acting on different immune system cells. Some of these cytokines are pro-inflammatory and may be a measure of the inflammatory response. Their measurement, however, is more tedious than the ESR, takes longer time, and is more expensive. Some of these cytokines are interleukin6 (IL-6), interleukin-1 (IL-1), and tumor necrosis factor-alpha (TNF-alpha). The future role of these glycoproteins in monitoring inflammatory conditions is uncertain due to expense but appears promising. Currently, the ESR is still the easiest and most convenient way to monitor such activity.”

Blood viscosity is an old measure of your health status not often obtained in modern medicine. Blood viscosity is a measure of the resistance of blood to flow. It can also be described as the thickness and stickiness of blood. The primary determinants of blood viscosity are hematocrit, red blood cell deformability, aggregation, and plasma viscosity. Unfortunately, the usual web sources on health, WebMD, Mayo Clinic, and Healthline, do not even discuss blood viscosity. Between 1950 and 1980, the NLM reports 833 articles with blood

viscosity in the article's title; between 2012 and 2022, 674 articles show up. Considering the explosion in scientific publications, nearly 2,000,000 per year now indicates a declining trend in studying blood viscosity as an important health marker.

Blood viscosity is directly related to the ESR measurement, Figure 5.3. Significantly, blood pressure is positively associated with viscosity. That is, as blood viscosity goes up, so does blood pressure. Increases in plasma protein cytokines, particularly fibrinogen, are primary determinants of plasma viscosity. When persistently elevated, are indicators of increased resistance to blood flow on the microcirculatory level and in arterial hypertension. Blood pressure increases trend with hematocrit, plasma viscosity, and red cell aggregation. Of course, ESR measures red cell aggregation and has a straightforward association with blood viscosity. Therefore, elevation in ESR – an easily modifiable biomarker – is a strong indicator of hypertension and thick blood.

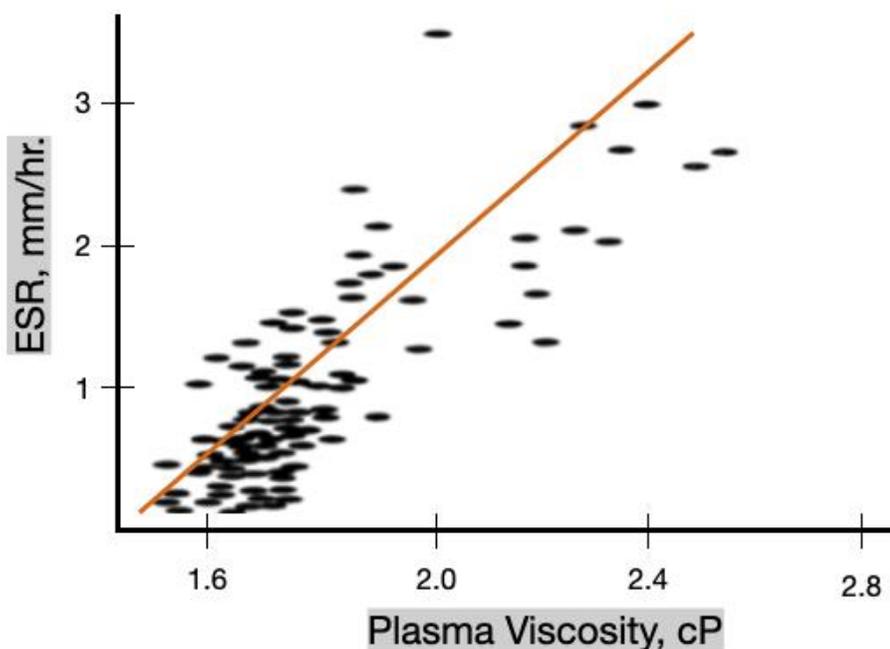


Figure 5.3. Correlation between blood (plasma) viscosity and the erythrocyte sedimentation rate (ESR).

Blood viscosity is an essential measurement of COVID-19. A report by Truong et al. from Emory University obtained blood viscosity measurements from patients with COVID-19 based on the known increase in clotting factors in the disease using several biomarkers, including D-Dimer.¹⁸⁸

“We were unsettled by the fact that some patients with severe COVID-19 had atypical blood clots, even when therapeutically anticoagulated,” says

Chapter 5. Electricity, Infection, and Malnutrition

Cheryl Maier, Assistant Professor of Coagulation and Transfusion Medicine, Department of Pathology and Laboratory Medicine, Emory University School of Medicine and medical director of Emory's Special Coagulation Laboratory. "Despite prescribing medications to prevent blood clots to COVID-19 patients, clotting still occurred, which is quite unusual," says Maier. "One thing that stood out was the extremely high levels of fibrinogen, a big sticky protein that increases with inflammation and is a key building block for making blood clots."

This team considered other causes of clot formation, like hyperviscosity, which can be detected by plasma viscosity (P.V.) testing. Hyperviscosity syndrome, where the high viscosity leads to dangerous sludging of the blood in the brain and other organs, produces viscosity levels similar to those seen in the sickest COVID-19 patients.

"We found that the sickest patients with COVID-19 had the highest P.V. levels, more than twice normal levels," says Maier. "We also found that patients with the highest viscosity levels were more likely to have a blood clot. We think the inflammation caused by SARS-CoV-2 infection causes hyperviscosity, which may contribute to blood clots in some patients." They showed an improvement in parameters by therapeutic plasma exchange (TPE). TPE is a procedure in which the patient's blood is passed through an apheresis machine, where the filtered plasma is removed and discarded with reinfusion of red blood cells along with replacement fluid such as plasma or albumin into the patient.

The ESR value is also severely elevated in COVID-19 patients and is most likely a low-cost measure of excess fibrinogen, D-Dimer, and clotting.¹⁸⁹ Interestingly, in this paper, the authors explain that the ESR value remains high long after COVID-19 appeared to pass. Future studies are needed to look at clotting factors in people who are no longer symptomatic. The elevated ESR, but in people no longer having COVID-19 symptoms, may explain sudden death in athletes who received the COVID-19 injection.

What enables red blood cells to defy gravity?

We know that red blood cells have a negative charge, which is why they resist settling. Like charges repel each other, and opposite charges attract. Thus, two negative charges repel one another, while a positive charge attracts a negative charge, but this is not the entire story. The cell membrane is a lipid bilayer that allows the flow of ions (in human physiology, ions are called minerals) through their ionic pumping proteins. Moving charges generate a current and a perpendicular magnetic field. Thus, in addition to the flow of minerals creating repulsion due to like charges, the magnetic field also causes repulsion between cells.

The flow of minerals into and out of cells is vital to circulation and health. In large arteries, blood travels quickly to nourish and detoxify tissue, initially at three feet

per second. As the arteries branch to service peripheral tissues, blood flow slows. All the important action occurs within the capillaries where a blood cell stops to deliver its load and pick up the waste and recyclable materials. Capillaries are tiny, thin blood vessels that connect the arteries and the veins. Their thin walls allow oxygen, nutrients, carbon dioxide, and waste products to pass to and from the tissue cells. It takes less than 60 seconds for a red blood cell to travel around the body. Think of it by way of this analogy: you are taking a trip and need to get to the airport. You start on a highway and then take progressively more minor roads with lower speed limits to reach your destination. Finally, you arrive, and the vehicle stops. There you get out and grab your luggage. On the way back home, you reverse this route.

The clumping of red blood cells causes health issues by slowing blood flow and creating blockages. Healthy red blood cells do not touch each other, or the vessel lining and efficiency flow through your bloodstream with minimal friction. The RBCs behave like cars; the drivers avoid collisions by keeping a distance between vehicles. More importantly, clumping of blood is a sign of severe underlying imbalances in physiology. For example, it may be a sign of a compromised sodium-potassium pump. The ESR is the best biomarker to assess this system's health.

The sodium-potassium pump is the enzymatic process that produces a charge and the electrical potential of a cell. Every single cell is a miniature battery charged by the flow of minerals. Not only does the sodium-potassium pump produce a charge, but the transformation of ATP into ADP also occurs, releasing (providing) energy to the cell. This process's ATPases (enzymes) are essential in all known life forms and have fundamental roles in energy production, active transport, and pH balancing. The ESR value is a reflection of how well these processes are functioning.

The ESR biomarker is a measure of cellular energy. This explains why the ESR might be the best biomarker test to obtain if you can get one.

According to Tishkowski¹⁸⁵, the following diseases are associated with an elevated ESR:

- Anemia
- Arteritis
- Infections (including bone and joint)
- Kidney disease
- Low serum albumen
- Lupus
- Lymphoma
- Multiple myeloma
- Polymyalgia rheumatica
- Red blood cell abnormalities

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- Rheumatoid arthritis
- Systemic vasculitis
- Thyroid disease
- Waldenstrom macroglobulinemia

The list below, from a National Library of Medicine search, shows additional diseases associated with an elevated ESR, not included in the Tishkowsky list, with the number of references in parenthesis:

- Stroke (26,800)
- Heart disease (36,700)
- Hypertension (48,200)
- Diabetes (57,400)
- Alzheimer's (5,040)
- Autoimmune disease (54,000)

Clinically, many comorbidities are observed in people with elevated ESR. The most common complaints observations include some type of gut dysbiosis (constipation, diarrhea, bloating, and GERD) and poor healing dependent upon certain mineral-containing enzymes.

Essentially all chronic diseases are impacted by blood flow, electricity, and cellular energy production.

We still have not worked back to the actual cause(s) of an elevated ESR. Inflammatory cytokines with positive charges can dampen the negative charges on cells and cause an increase in the ESR value. And the flow of minerals through active transport creates the cellular charge and perpendicular magnetic force. However, another mechanism not found in published literature may also be in play – a mineral deficiency. Suppose minerals involved in the active transport (the sodium-potassium pump) create the charge and magnetic force. In that case, it only makes sense that a mineral deficiency could also be related to an elevation in the ESR.

Magnesium is required to transport ions, such as potassium and calcium, across cell membranes. Magnesium affects the conduction of nerve impulses, muscle contraction, and normal heart rhythm through its role in ion transport systems. About half of the U.S. adult population may have insufficient magnesium intake to support nutritional adequacy. The Linus Pauling Institute provides an excellent summary of active transport and minerals critical to its optimal function.¹⁹⁰

“Sodium and chloride are electrolytes that maintain concentration and charge differences across cell membranes. Potassium (K⁺) is the principal positively charged ion (cation) inside cells, while sodium is the principal cation in extracellular fluid. Potassium concentrations are about 30 times higher inside than outside cells, while sodium concentrations are more than ten times lower inside than outside cells. The concentration differences between potassium and sodium

across cell membranes create an electrochemical gradient known as the membrane potential. A cell's membrane potential is maintained by ion pumps in the cell membrane, especially the Na⁺/K⁺ ATPase pumps. These pumps use ATP (energy) to pump sodium out of the cell in exchange for potassium. Their activity has been estimated to account for 20%-40% of the resting energy expenditure in a typical adult. The large proportion of energy dedicated to maintaining sodium/potassium concentration gradients emphasizes the importance of this function in sustaining life. Tight control of cell membrane potential is critical for nerve impulse transmission, muscle contraction, and cardiac function.”

Mild sodium deficiency is becoming more common with doctor recommendations for low sodium diets. Sodium is involved in hypertension while being extraordinarily important in physiology. According to Harvard Medical School, hypertension “caused” by sodium is often actually the result of potassium insufficiency rather than an excess of sodium.¹⁹¹ Most people have properly working kidneys; thus, consuming sufficient or modest excesses of these fundamental nutrients does not impact blood pressure. The human body is intelligent and regulates concentrations regardless of intake – as long as there is sufficiency.

Potassium is arguably the most neglected of the critical minerals. Estimates of Americans who are potassium deficient range from 50 to 98 percent. Not surprisingly, it is classified as a “nutrient of public health concern” according to the 2015-2020 Dietary Guidelines for Americans since its underconsumption in the U.S. population is associated with adverse health effects, including hypertension and cardiovascular diseases.¹⁹²

Sodium, potassium, magnesium, and chloride are not the only substances involved in active transport. Enzymes are foundational to physiological processes, including active transport. Many enzymes only function correctly in conjunction with minerals, often called trace minerals. Trace minerals involved in enzymatic processes include, but are not limited to, copper, iron, manganese, molybdenum, selenium, and zinc.

The bioavailability of micronutrients is not well understood. In general, a scientific understanding of uptake, absorption, and bioavailability in humans is still at a nascent stage. An article titled “Bioavailability of Micronutrients From Nutrient-Dense Whole Foods: Zooming in on Dairy, Vegetables, and Fruits”¹⁹³ explains this: “Not all micronutrients are well absorbed, even in healthy people. For example, Green leafy vegetables are rich in iron, but the bioavailability of iron is relatively low—around 12%. The low bioavailability is attributed to the indigestibility of cellular components such as chloroplasts and mitochondria where iron is stored.” This percentage will be less in people with any level of gut dysbiosis. Based on clinical observation, only a tiny percentage of our population has a truly optimal gut. Thus, many have poor absorption of micronutrients and the myriad of disease processes associated with this deficiency.

The ESR, when elevated, is an indicator of the risk of dying prematurely. Dozens of peer-reviewed medical publications assert this relationship. A couple of examples are provided below:

“Erythrocyte sedimentation rate: a possible marker of atherosclerosis and a strong predictor of coronary heart disease mortality.”¹⁹⁴ “The erythrocyte sedimentation rate is a strong predictor of coronary heart disease mortality and appears to be a marker of aggressive forms of coronary heart disease. The erythrocyte sedimentation rate probably gives substantial information in addition to that given by fibrinogen on the risk of coronary heart disease death. Nevertheless, a high-risk group can be defined by an erythrocyte sedimentation rate >15 mm/hr.” Note that the standard of care considers ESR normal in the range of 0 – 40 mm/hr.

“Elevated Erythrocyte Sedimentation Rate Is Predictive of Interstitial Lung Disease and Mortality in Dermatomyositis (D.M.): a Korean Retrospective Cohort Study.”¹⁹⁵ “Elevated ESR is associated with increased mortality in patients with D.M. due to respiratory failure. Thus, monitoring ESR should be an integral part of the clinical care of D.M. patients.”

Erythrocyte sedimentation rate as an independent prognostic marker for mortality: a prospective population-based cohort study.”¹⁹⁶ “We studied data from the Rotterdam Study (1990–2014). ESR levels were measured at baseline and following individuals until death or the end of the study. Associations between moderately (20–50 mm/hr.) and markedly (>50 mm/hr.) elevated ESR levels and all-cause mortality was assessed using multivariate Cox proportional hazard models. An elevated ESR is an independent prognostic factor for mortality. Even though ESR increases with age, it remains associated with an increased risk of mortality and warrants close follow-up.”

The Rotterdam Study is well respected, and this paper is a landmark. Shockingly, the report has only been cited three (3) times in the medical literature, reflecting a lack of appreciation for the value of this biomarker in clinical medicine. Figure 5.4 shows the correlation between ESR and mortality. The <3 line in the figure is an added to show an estimate of projected mortality trends when ESR is optimal.

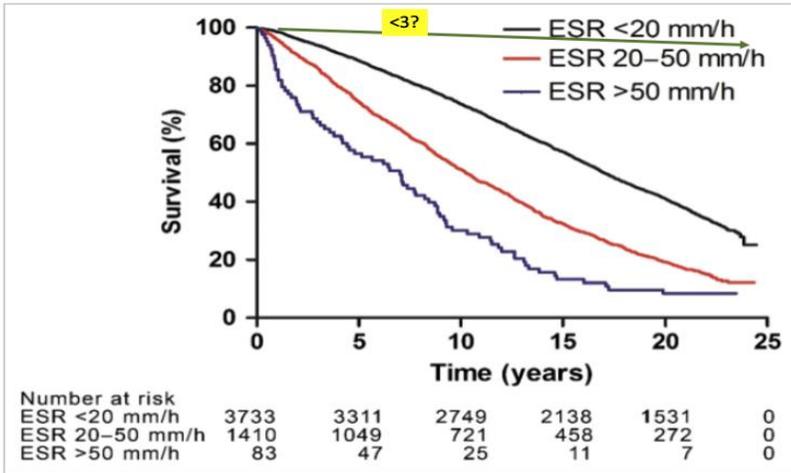


Figure 5.4. ESR values and early mortality (survival) percent. The optimal value for ESR is <3. That line was added to the figure by the authors of this book.

The point of this entire section is to show that the ESR is a profoundly important marker that bridges digestion, absorption, and nutritional decisions, to the health of your capillaries, electricity production, energy generation in the body, and the risk of dying young. This makes ESR arguably the single most important biomarker. Doctors used to measure ESR routinely. In a personal conversation with a group of doctors, two made the following statements about the ESR measurement:

“We used to measure ESR.”

“If ESR is elevated, we would not know what to do about it, so we do not measure it anymore.”

Chapter 6. Oral Health IS Whole Body Health

"You will observe with concern how long a useful truth may be known and exist before it is generally received and practiced on."

- Benjamin Franklin.

Oral Health IS Whole Body Health

Summary: Charles Mayo, the founder of the famous Mayo Clinic, professed over one hundred years ago that focal infection from the mouth would be the next great area of medical advancement. Unfortunately, this area of medicine is hardly on the radar of the Mayo Clinic today. A previous chapter discussed stealth infections as a causal factor in many chronic diseases. Oral infections, many of which go unnoticed and undetected, contribute greatly to the burden of stealth infections and chronic diseases.

The American Dental Association has taken away your health freedom because they promote root canals, amalgams, fluoride, and unnecessary teeth removal. The dental silo of healthcare is the only one that keeps a dead organ in your body. Do you think this is a good idea?

Your mouth is a source of subtle but chronic risk to your health. However, what appears on the surface is NOT what creates health problems. Yet, this is where most dental care occurs. Look upon your teeth like an iceberg. They can appear beautiful and white above the gum line like the ice of the berg glistening in the sunshine. However, below the surface, danger lurks. It was the part of the iceberg below the water that sunk the Titanic.

Here is a testimonial from a lady who went through our program and obtained blood testing along with a saliva test for oral pathogens.

"Hi, Dr. Lewis.

We had a consult a few weeks ago. My bloodwork revealed an underlying infection of some kind, so you recommended the MyPeriopath, on the hunch it could be a mouth infection. I did that and had some harmful pathogens in my results. I found a new dentist in my area that includes cone scans, and low and behold, and they found an infection in tooth #15 on the top. It had a crown from many years ago but had NOT had a root canal. The infection is pretty bad and even pushed into my sinus. Crazy, considering I have had zero pain in that tooth or sinus. It's been at least a year since I had that infection because I had bloodwork taken last

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December and had a high white blood cell count at that appointment. I'm so appreciative of your consult, as this infection would have continued to progress."

Her blood labs and oral testing results are provided in Figures 6.1 and 6.2., respectively.

Heart	WBC	RDW	Neutrophils	CRP	Homocysteine	Heart
Optimal	4000 - 5800	11 - 12.5	2000 - 3500	< 0.6	5 - 10	0 to 10 Scale
Value	6000	13.1	3500	4.2	12.2	2.9

Figure 6.1. Biomarkers for a person with periodontal infection. The white blood cell count (WBC) and neutrophil levels are considered normal in the standard of care. However, these slightly elevated levels indicate low-grade (smoldering) bacterial infection.

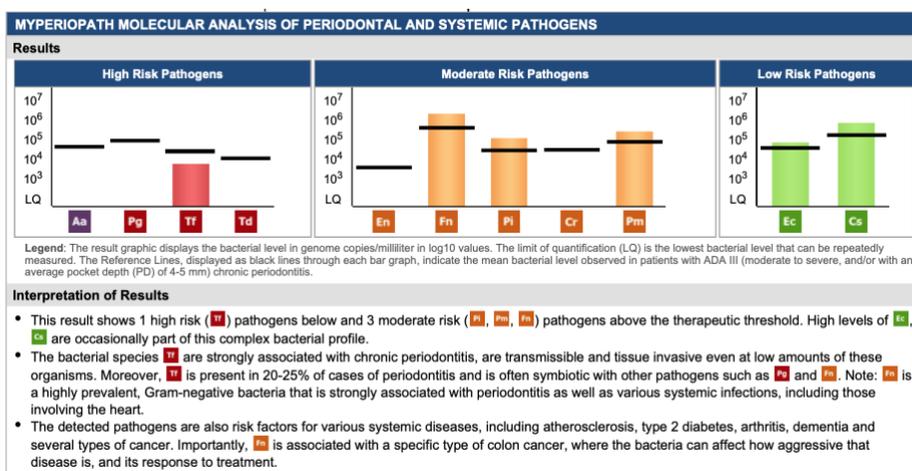


Figure 6.2. Oral pathogen test results. The "Fn" bacterium is considered harmful to the heart. Blood labs indicate elevation in CRP and homocysteine, which are markers of inflammation and heart risk.

Your regular dentist often misses these mild but significant infections. They do not include blood testing in their mouth analysis as if the mouth is not part of the whole. They are particularly ill-equipped to determine if you have an infection below the gum line. Most dentists take a 2-dimensional X-ray. The Cleveland Clinic explains that "X-rays detect decay between teeth and changes in the thickness of bone caused by gum disease" What they do not tell you is that the disease has to have progressed significantly before bone or tooth loss is detected. In the meantime, the infection that causes this has been smoldering, possibly for years. But it is just happening in the mouth, right? No need to worry except for these two facts.

On average, a red blood cell circulates through your entire body every 60 seconds (1 minute).

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A capillary, the smallest blood vessel, must be within three cell diameters of any viable cell.

The translation of this information is that the circulatory system interconnects our entire body. Therefore, the infection below the gum line, or anywhere, can easily travel from the teeth roots and gums to other parts of the body. And, based on blood flow, the pathogen has 1000 opportunities to circulate daily.

The biological dental community often uses a more advanced 3D X-ray device. This "cone beam" X-ray is an improvement compared to the 2D instrument with poor resolution. However, it is still an X-ray and is inadequate for early detection of oral diseases below the gum line. Vetter Dental adequately explains X-rays and the difference between the 2D and 3D varieties.¹⁹⁷

"A 2D x-ray is an x-ray examination that captures mouth images. This includes the teeth, upper and lower jaws, and surrounding structures and tissues. These x-rays can range from simple intraoral to extraoral full mouth x-rays."

"Unlike 2D x-rays, three-dimensional x-ray imaging was developed to help create an understanding of the entire mouth by designing a 3D rendition of the oral cavity. The 3D image captures a true 3d image of the mouth and allows the dentist to study the mouth in slices, similar to a CT scan. These x-rays are sometimes referred to as a cone beam, capturing images of the teeth and mouth."

Anyone over 50 with any type of oral symptoms should obtain a 3D x-ray and an oral saliva test for pathogens every couple of years.

Our lady from the testimonial indicated that the oral infection was pushing up into her sinuses. According to the Cleveland Clinic, an estimated 31 million people in the United States have sinusitis or inflammation of the sinuses.¹⁹⁸ Based on this testing, it is reasonable that a substantial cause of sinusitis is periodontal or gingival infections. Is the medical community looking for this cause/effect relationship?

Oral Bacteria and Alzheimer's Disease

Sinusitis is annoying but does not significantly impact health; however, Alzheimer's disease certainly does. A 2022 article explains that one of the most feared diseases starts in the mouth. The title of the paper is "Alzheimer's starts in the mouth? Gum disease, oral bacteria strongly linked to the mind-robbing condition."¹⁹⁹ The website quotes a group from Tufts University that published a scientific paper on the topic.

"Researchers from the Tufts University School of Dental Medicine suggest a link between a common bacterium that promotes the progression of periodontal disease and Alzheimer's disease. Jake Jinkun Chen, professor of periodontology and director of the Division of Oral Biology at Tufts

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University School of Dental Medicine, and his colleagues believe that targeting *Fusobacterium nucleatum* (*F. nucleatum*) can kill two birds with one stone, slowing the progression of both diseases."

Researchers have recently linked *F. nucleatum* to conditions ranging from premature baby delivery to colorectal cancer. In the case of periodontal disease, the bacteria impact the gums and jaw. If left untreated, it can result in loose teeth and lost teeth. It can also exacerbate inflammation, a symptom of most chronic diseases like Type 2 diabetes and cardiovascular disease.

In Chen's latest research, experiments revealed the relationship between bacteria and microglial cells. These are immune cells within the brain that remove damaged neurons and maintain the health of the central nervous system. Mice were used to conduct the experiments, and *F. nucleatum* caused abnormal growth of microglial cells.

Due to an increase in these cells, the body seemed to respond by increasing inflammation. Chronic inflammation is considered key in determining neurodegeneration progression in Alzheimer's disease patients. "Our studies show that *F. nucleatum* can reduce the memory and thinking skills in mice through certain signal pathways. This is a warning sign to researchers and clinicians alike," Chen said.

And my favorite quote...

"In this study, our lab is the first to find that *Fusobacterium nucleatum* can generate systemic inflammation and even infiltrate nervous system tissues and exacerbate the signs and symptoms of Alzheimer's disease," adds Chen.

Claims of unique discoveries are typical of academic bravado. Researchers frequently claim to be the first to make some discovery, no matter how minuscule. That is how they maintain funding. But their claim is entirely false. They were scooped by at least 200 years. More importantly, their work has just been on mice. Craig Atwood is a researcher known for publishing peer-reviewed articles with provocative names. My favorite is "Living and Dying for Sex."²⁰⁰ In another publication, he showed very clearly, how the mouse model is invalid in Alzheimer's studies.²⁰¹ Dr. Ewald, highlighted in Chapter 5, explained the same thing. So much for the Tufts University bravado.

Let's look at who scooped the Tufts researchers.

Benjamin Rush, M.D.: Doctor Rush signed the Declaration of Independence. In 1806 he stated, "As a medical doctor, I am just another contributor to the knowledge that, when an infected tooth is removed from a patient, their general health improves."

Charles Mayo, M.D.: Dr. Mayo was the founder of the famous Mayo Clinic. In 1913, he made a major presentation at the dental society meeting in Chicago. He declared that managing oral infectious would be the next and most important

medical technology and disease prevention phase. He promoted the concept of "focal infection." This term means localized infection. When the focal oral infection is in the elbow, we call it arthritis. When the focal oral infection is in the brain, we call it dementia or other brain ailments.

Judith Miklossy, M.D., Ph.D.: Dr. Miklossy, over the past 30 years, has performed the most scientific evidence-based work on the connection between oral pathogens and systemic diseases, with a focus on those of the brain. Her first publication on this topic in 1993 is titled, "Alzheimer's, a Spirochetosis?"²⁰² She has subsequently proven the spirochetal infection is a cause of dementia beyond any reasonable doubt.

Medical leaders are not reasonable, however. "Beyond any reasonable doubt" only matters if it fulfills a specific agenda. Here is the summary of her 1993 paper.

"Here I report observations that in 14 autopsy cases with histopathologically confirmed AD, spirochetes were found in blood and cerebrospinal fluid and could be isolated from brain tissue. Thirteen age-matched control cases were without spirochetes. In addition, reference strains of spirochetes and those isolated from the brains of AD patients showed positive immunoreaction with a monoclonal antibody against the beta-amyloid precursor protein. These observations suggest that spirochetes may be one of the causes of AD and may be the source of the beta-amyloid deposited in the AD brain."

Whence do spirochetes come? There are three (3) categories of spirochetes Treponema, Borrelia, and Leptospira. They come from tick bites (Borrelia), through direct contact with urine from infected animals or through water, soil, or food contaminated (Leptospira), unprotected sex (Treponema), and from the mouth (Treponema Dentacola as an example).

Lyme disease from tick bites that deliver Borrelia is relatively common. Borrelia and other spirochete species cause acute illness, and the CDC vacillates between, indicating that there are 30,000 to 300,000 active cases in the United States. Functional doctors who focus on Lyme syndrome disease believe that up to 20 percent of Americans with chronic disease are infected with a tick-based spirochete. Functional doctors are both right and wrong. However, the CDC is 100% wrong as they infer chronic diseases result from a deficiency in some drugs. Lyme disease is a misnomer and does not convey the association between spirochetal infections and chronic diseases.

- "Lyme" disease is highly prevalent but underappreciated as a cause of many chronic conditions.
- Lyme is a town in Connecticut where ticks are prevalent and is the reason for the name "Lyme disease." However, Lyme disease should be considered an umbrella category for any condition involving a spirochetal infection.

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- The most prevalent cause of "Lyme Syndrome" is actually *Treponema* spirochetes or other pathogens derived from periodontal disease of the mouth, NOT from a tick bite.

A proper translation of Dr. Miklossy's 1993 paper becomes.

Alzheimer's is a spirochetal infection mainly derived from the mouth.

The researchers from Tufts indicated that Alzheimer's might be caused by *Fusobacterium nucleatum* (FN), which is not a spirochete. Instead, it is a Gram-negative, anaerobic oral bacterium. Does it really matter? Pathogenic infectious species like spirochetes and gram-negative bacteria may cause harm in a compromised host and trigger an inflammatory immune response. There are several factors when determining how vital a bacterium is in causing disease, including virulence, physiological kinetics, and the internal terrain of the infected person. SARS-CoV-2 helped cement the relationship between outcomes and the vulnerability of the person infected.

The Tufts researchers, like most academics, practice reductionism. They focus and specialize on one thing to carve out a niche. However, a single periodontal infection like FN rarely occurs in the real world. The host, the person with FN, is vulnerable not just to the FN but also to other opportunistic infections. OralDNA Labs is one of several labs that test for oral pathogens. Specifically, they test for 11 unique oral pathogens. Their scientists state these 11 are just the "usual suspects," and many more lurking in your mouth and body. Figure 6.2 above is an example report produced by OralDNA labs. Figure 6.3 is also an OralDNA report that provides the names of the 11 usual suspect bacteria.

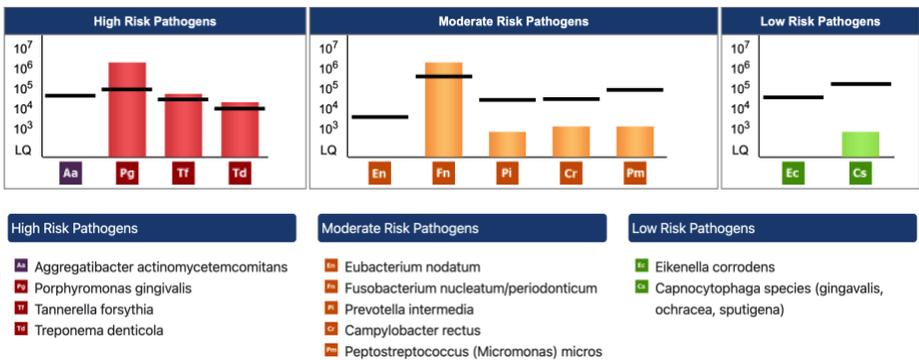


Figure 6.3. Example OralDNA report including the names of eleven common oral pathogens.

According to those who study the virulence of oral pathogens, FN is of only moderate risk to your health, while the spirochete, *Treponema Dentacola*, is high risk. Blood testing for Lyme disease may include a "Lyme, Line Blot" for

spirochetes. Commonly, bands for "Lyme" appear on this blot but are not in sufficient numbers for the labs to indicate an individual is positive for Lyme disease. However, our clinical work reveals that those with a spirochete in the OralDNA test usually have one or more Lyme Line Blot bands classified as abnormal, Figure 6.4. The conclusion drawn from these two data sources is the oral spirochete(s) are cross-reacting in the serum blood test. The association between the OralDNA test and the Lyme test is strong.

▶ IgG P41 Ab. ⁰²	Present	Abnormal	Absent	12/21/2021
IgG P39 Ab. ⁰²	Absent		Absent	12/21/2021
IgG P30 Ab. ⁰²	Absent		Absent	12/21/2021
IgG P28 Ab. ⁰²	Absent		Absent	12/21/2021
▶ IgG P23 Ab. ⁰²	Present	Abnormal	Present	12/21/2021
IgG P18 Ab. ⁰²	Absent		Absent	12/21/2021
Lyme IgG Line Blot Interp. ⁰²	Negative		Negative	12/21/2021

Figure 6.4. Lyme, Line Blot, Serum for an individual with a spirochete at moderate levels in the OralDNA test.

I used to have high expectations for my Alma Mata MIT and other academic institutions, but that has long been extinguished because of their paltry contributions to community and population health. MIT has a center focused on brain health, and they also participate in Harvard and MIT collaborations. If these distinguished places cannot solve the world's problems, who can?

Here is an example of how I lost faith in the academic research world. Do not get me wrong; brilliant work is ongoing. But here we are well into the 21st century, and over 60 percent of U.S. adults have at least one chronic condition. So what the heck are all these academic research centers studying? At best, very little that impacts your health.

Here are two examples:

Example 1. My advisor at MIT was the youngest Chaired Professor in the history of MIT. Quite a prestigious accomplishment. He then went on to be Chancellor of Washington University in St. Louis. I noticed that the Washington U. medical school published some exciting articles on Alzheimer's. So, I called Mark, my former advisor, and discussed what I knew about the spirochete / Alzheimer's connection. He was intrigued and informed me that his university had several "molecules" in the pipeline.

Molecules, of course, mean pharmaceuticals. You can be sure none of those "molecules" treat spirochetes of the mouth. Instead, there were being developed to treat Tau and Amyloid, which are protective against Alzheimer's. If you are waiting for an Alzheimer's cure, it will be a long time for academia to move away from the failed models. The Titanic comes to mind again. It turned so slowly it could not avoid the iceberg. Academic research is quite similar in its agility.

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Science and, more particularly, medicine changes very slowly. A famous nuclear researcher, Max Planck, famously stated,

"Science advances one funeral at a time."

Example 2. Doctor Burke introduced me to Dr. Trempe, and we would spend time together at MIT and Harvard. We attended conferences and lectures and participated in the MIT Enterprise Forum. One day I took him for a tour of MIT Nobel Prize Laureates, who were surprisingly receptive to our unannounced visits.

Two of MIT's brain centers are The McGovern Institute for Brain Research and The Picower Institute for Learning and Memory. High-powered stuff. Dr. Burke and I managed to get an audience with the director of the McGovern Institute by being general nuisances. We were granted an hour and explain our infectious hypothesis and approach to Alzheimer's. We even had videos of some of Dr. Trempe's patients who had evident dementia and showed remarkable improvement after treatment, something not achieved by the MIT brain trust. The director was interested, and we offered to consult with the Institute with no expectations and at no cost. Dr. Burke was wealthy and just wanted to contribute to solving this disease. Unfortunately, we did not hear back from McGovern after several calls to determine the next steps. This occurred around 2010.

Fast forward several years, I read something from MIT that caught my eye. The first was a publication in "Spectrum" magazine, where a dean indicated their group was the first to identify inflammation as a causal factor in Alzheimer's. So I wrote everyone involved in that article and the President at MIT a pleasant email that explained they were scooped by 200 years - just like our Tufts researchers.

Next, I read an article from the Picower Institute. Here is a summary of that news flash. "How dementia begins and progresses is still a mystery," said Picower Professor Li-Huei Tsai, who heads MIT's Picower Institute for Learning and Memory and the Aging Brain Initiative. "And to solve that mystery requires a completely different approach."

You guessed it. The new approach has nothing to do with spirochetes. So what is this new approach? Here is their summary.

"In collaboration with MIT Professors Edward Boyden '99, MNG '99, and Emery Brown, Tsai found that they could stimulate gamma waves in the brains of mice with Alzheimer's disease by exposing them to lights flashed on and off at a particular frequency, about 40 cycles per second. The light signals activated the brain and trained neurons to fire at gamma frequencies."

Many faculty and fancy people at MIT got another email from me that read, "Indeed, Director Tsai, the only difference between today and 150 years ago when

there were very few incidences of Alzheimer's is the cycling of light. That is it! Brilliant! Alzheimer's will finally become history!

My sarcasm increased as I realized MIT would not solve Alzheimer's and neurodegeneration. Hopes dashed that my Alma Mata was creating the value I expected.

The rest of my email read, "Dr. Trempe and I discussed our program with the head of the McGovern Institute²⁰³ to crickets! Sadly, like the rest of the world, MIT is only interested in treatments they can license for large sums of money." Do you think this is a bit harsh? Then why do I not see MIT technology making a real difference in people's lives in East Cambridge and around the globe? Why do research just for the sake of research? Because it is how researchers put food on the table!

None of the Ivory Tower academics at MIT responded to my emails. Next, I got this note from MIT in my email. "It is with profound sadness that I share the news that Paul Gray, MIT's 14th president - and one of the finest men I have ever known - passed away this morning, surrounded by family, after a lengthy battle with Alzheimer's disease. He was 85."

Ineffectual science occurs when you perform research in a vacuum and ignore the obvious and less elegant science, like periodontal pathogens. No one is exempt from a disease like Alzheimer's, regardless of their stature. Look at Reagan, Biden, and Paul Gray - the head of MIT. Picower and McGovern Institutes have billions of dollars at their disposal and could not slow or stop Dr. Gray from suffering through a lengthy battle with Alzheimer's.

The good news is, you can. This simple place to start, by taking care of your mouth, puts you way ahead of the research at MIT and Harvard. Do NOT get root canals. If you have one or more, have them pulled. If you have had wisdom teeth removed, check for cavitations and treat them aggressively. Remember that your dentist - even a biological dentist - will not treat you systemically for oral pathogens. These organisms can migrate to other tissues like your heart or brain. Find the rare functional doctor who understands the risks associated with systemic periodontal bacteria and how to treat them to reduce risks and reverse diseases caused by these stealth organisms.

Functional Periodontist on Oral Health

Your mouth and gut are the two most important areas to focus on if you want to live a long and healthy life. Indeed, the mouth is considered to be part of the gut. However, even though each is part of the same system, how they impact health differs substantially.

Your regular dental visit is mainly with the hygienist that does the cleanings. It is vital to get these done regularly. However, you should also follow the program for home oral hygiene provided at the end of this chapter because the ADA

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protocol has nothing to do with the highest risk the mouth presents to your health - spirochetes and other infectious species. The ADA is all about two things only.

- Preserving enamel (drill and fill);
- Saving the tooth regardless of the cost to your long-term health.

Neither of these is your priority.

Your regular dentist looks below the gum line, where most infectious action occurs. However, they use a 2-dimensional X-ray with an insufficient resolution to see the early or mild infection. The X-ray can determine bone loss. However, bone loss means infection and inflammation are highly active. Therefore, if you have bone loss per a 2D X-ray, you are well down the wrong end of the oral health-disease continuum.

Dr. Patricia Berube is a periodontist. However, she is carving out an entirely new category, that being a "functional" periodontist. The term "functional" or "integrative" in medicine differentiates a traditional doctor who treats symptoms from an advanced doctor who explores for and treats causes. Dr. Berube views the periodontal arena the same way. Her goal is to solve issues of the mouth in strict consideration of health issues impacting your entire body. Dr. Berube was kind enough to provide insights into her approach to better oral care.

"As a periodontist, I'm very aware of the discussion of dental disease and its role in systemic disease. For decades, this subject has been written about extensively in the scientific literature but seldom carried over into the mainstream. However, if this is not a new topic, how long ago did it first appear, or more specifically, how long ago has there been evidence that disease in the mouth can affect the rest of the body?"

Charles Mayo, MD, one of the founders of the Mayo Clinic, spoke in front of the Dental Society of the State of New York in 1922 titled, "Focal Infection of Dental Origin." In this excerpt, he began by describing how infections of the jaws have been shown to go back five thousand years before Christ and that even Hippocrates recorded two cases in which the removal of mouth infections had relieved patients of rheumatic troubles of the joints.

Dr. Mayo described how he "pulled" teeth at one point in his career and was amazed at the conditions cured after removing the infections from the mouth. However, he was unequivocal in stating that "in the mouth will be found evidence of more diseases than in any other region of the body; such evidence will be in the form of nutritional changes, and infections around the gums, teeth, and in the tonsils." Therefore, he believed that dentists must lead preventative medicine.

One of the oldest conditions known to man is an infection of the jawbone. Although this condition has been given many names over the years, the most current is human jawbone osteonecrosis. It was discussed back in 1868 by Noel and in 1901 by Barrett describing defects found in the jawbone. Even G.V. Black

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discussed this in his 1915 textbook, discussing the appearance and treatment options for jawbone osteonecrosis.

Fast forward a few decades, and we cannot continue the discussion without mentioning the work of Dr. Weston A. Price. He spent most of his career studying the effects of root canals on teeth and found that all root-canaled teeth were infected. His publication, "Dental Infections, Oral and Systemic," was used as a reference in textbooks in the 1930s. He then began focusing on nutrition, and in 1939, he published the book, "Nutrition and Physical Degeneration." This book is a fascinating study and conclusion to his many years of travel worldwide to find the cause of dental disease.

Why was it that "savage" people had beautiful disease-free teeth and "civilized" men did not? Through his travels, he found that indigenous people that stayed true to their native diets had wide dental arches with no crowding and a lack of dental cavities and periodontal disease. When the parents strayed from the native diet and started adding items from the Western diet, such as white flour and white sugar, they began to see malocclusion, narrowing of the face, and dental disease. In their native diets, calcium and minerals consumed were four times greater, and their fat-soluble vitamin intakes were ten times greater than in "civilized" society.

Humans all seem to walk around with their heads firmly planted on their bodies. We don't think twice about this, yet dentistry turned into a carpenter's type of trade. Effects on the remainder of the body were not considered. Many examples include using amalgams to replace lost tooth structure, root canals to "save" a tooth, and the seemingly routine removal of wisdom teeth. All of these procedures are provided by dentists that are non-suspecting of the ill effects they may provide. After all, if it was taught in school, it must be the right way. Like many physicians that wake up to realize their training was sorely lacking, some dentists realized the ill effects of these procedures. However, the standard of care in dentistry forces them to perform these procedures in order to get paid.

The payer system stymies the practice of dentistry.

Functional Periodontist's View on Mercury Amalgams

Dental amalgam is an "amalgamation" of about 50% mercury, silver, copper, tin, and zinc. We call these "silver fillings" because of their appearance. Installing fillings is one of the more basic methods taught in dental school, with the removal of tooth structure needed to hold the filling in place mechanically. For many years this material was deemed safe in the mouth. However, now some dentists understand the ill systemic health effects that occur as a result of mercury amalgam.

Many books, position papers, and organizations advocate removing amalgams in dentistry. While there are recommendations to eat less fish, stop using mercury thermometers, and remove mercury from vaccines, it is curious why this toxicity doesn't raise a red flag when it is placed in the mouth, just centimeters away from

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the brain. The political battle over amalgams in the United States has been going on for decades. While there have been small victories here and there, the most notable has come in a recent update from the FDA recommending specific "high-risk" individuals to consider other types of restorations that could be safer. There have also been more laws governing dental offices to install appropriate mercury disposal systems. While many practitioners are weary of yet another regulation, they fail to see that these disposal systems are safer for them, their staff, and our environment.

The International Academy of Oral Medicine and Toxicology (IAOMT) is considered the foremost society of biological dentists. They offer a site titled "Dental Amalgam Mercury Fillings and Danger to Human Health."²⁰⁴ The associations between mercury and disease are presented in Table 6.1.

Allergies	Alzheimer's disease	Amyotrophic lateral sclerosis (Lou Gehrig's disease)	Antibiotic resistance	Autism spectrum disorders
Autoimmune disorders/ immunodeficiency	Cardiovascular problems	Chronic fatigue, fatigue, myalgic encephalomyelitis/ chronic fatigue syndrome	Complaints of unclear causation	Dermatitis
Fibromyalgia	Gastrointestinal issues and/or irritable bowel syndrome	Hearing loss	Kidney disease	Multiple sclerosis
Oral lichenoid reaction and oral lichen planus	Orofacial granulomatosis	Parkinson's disease	Periodontal disease	Psychological issues such as depression and anxiety
Reproductive dysfunction	Suicidal ideations	Symptoms of chronic mercury poisoning	Systemic lupus erythematosus	Thyroiditis

Table 6.1. List of diseases associated with dental mercury amalgams. The IAOMT assembled this list. It includes peer-reviewed references for each condition. See www.iaomt.org.

When so many more benign materials are available, is this something you want to take a chance on?

The first step is not to have any amalgams placed in your mouth. If amalgams are already present and you have systemic disease, removing them could be an option to help improve your health. Removal should be performed by a certified dentist who will use the proper precautions for themselves, their staff, and you during the procedure. Heavy metal testing and detoxification are essential long-term health considerations.

Many patients come in and ask if they should have their amalgams removed. The answer is not a simple yes or no. If they are healthy, with no evidence of systemic disease, and the patient cannot afford the removal, I am more hesitant to say yes than if someone is very sick and has tried many different avenues of healing.

Removing a large amalgam can severely compromise a tooth. Informed consent in dentistry involves understanding the risks of amalgam removal that may improve your health. Too often, when an amalgam is removed, the area drilled is too deep. In these instances, the tooth requires a root canal. This creates an even more severe health problem, affording the dentist a substantial payment for services.

Functional Periodontist's View on Root Canals

Root canal therapy is a widely debated topic as well. More and more studies have documented the role of oral microbes and their initiation and link to the progression of conditions such as cancer. We can come back again to the Weston A. Price studies that showed that placing root-canaled teeth in rabbits caused every rabbit to become sick with the disease of the person with the infected tooth. However, after the removal of the tooth, the rabbits recovered. The evidence is quite compelling and jarring.

Another book that discusses root canals at length is called "The Root Canal Cover-Up" by Dr. Meinig. The question is whether a tooth root can become 100% free of bacteria due to a root canal procedure. Also, what are the consequences of disturbing the balance within and beyond the structure when bacteria remain? The theory is that the bacteria give off toxins and continually infect the surrounding bone and vascular system, traveling to other body parts.

It is not uncommon for root-canaled teeth to be very brittle and infected. I rarely remove a root-canaled tooth that doesn't have some sort of apparent acute or chronic infection, regardless of its age. Microscopic examination has shown multiple toxic bacteria associated with these teeth. The OralDNA test also illuminates the presence of periodontal bacteria.

There are also many case studies and anecdotes of patients who note that after removing their root-canaled teeth, one or more of their symptoms improved. One frequent benefit is an improvement in energy levels. These stories of health improvement are compelling. However, many sinus symptoms improve upon removing teeth adjacent to a sinus. If this is the case, what about those root-canaled teeth that are not adjacent to a sinus? Do the bacteria stay within the periodontal ligament of that tooth, or is it possible they seep into the adjoining jawbone or tissues? Studying these effects is very difficult, but it seems as if performing randomized, double-blind studies (the gold standard of studies) on root canal removal and health improvement would shed some light on this subject.

Individual case studies in clinics worldwide may not be written up and published. Still, they are no less essential to understanding how dental procedures and materials can affect the body. I hope that diagnostics become available to clinicians to evaluate for toxicity. One example is a test called orotox that measures the toxic hydrogen sulfide compounds emitted from bacteria around root-canaled teeth.²⁰⁵ Another test is the Mercaptans/Thioether Sensitization Test,

which detects immune and inflammatory reactions to the bacteria around root-canaled teeth.²⁰⁶ Although not available commercially, be watchful as they hopefully will be available soon.

Dr. Levy has a great discussion in his book, "Hidden Epidemic: Silent Oral Infections Cause Most Heart Attacks and Breast Cancers." He distinguishes between an infected tooth that is not treated versus a root-canaled tooth. Which is the healthier option? According to Dr. Levy, the tooth left with an infection will have a more deleterious effect on your health. Therefore, leaving an infected tooth is not an option. A challenge emerges because many people do not know that they have a time bomb in their mouths. As a result, they feel no pain or discomfort.

Many patients decline a complete mouth series of radiographs (the standard of care) due to fear of radiation. This is not prudent, in my opinion. Viewing the entire root is the only way to confirm if there is an infection. Without proper imaging, your dentist is blind. The question then arises as to if you should have a root-canaled tooth removed. Again, are you healthy, or are you sick? Have you had a CBCT 3D dental scan to evaluate the bone around the root canaled teeth? CBCT scans can detect changes in the bone that our 2D images cannot see.

While a root-canaled tooth may appear healthy on a 2D image, a 3D image may show the true extent of the infection. These silent, chronic infections or "abscesses" are considered benign if there are no symptoms. We are finding that this is not the case. Informed consent is the key to this process, with the understanding that removing a tooth should be discussed at length, with considerations for replacement. There is disagreement, even in the biological dental community, about the best way to replace a tooth. Some say it is best not to replace the tooth, some say it's best to prep the adjacent tooth and fabricate a bridge, and others say replacement with ceramic implants is the best option. Again, informed consent is paramount.

Other procedures performed routinely include wisdom tooth extraction or just tooth extraction in general. Many factors can contribute to incomplete healing of the tooth socket, both endogenous and exogenous, as well as pharmaceutical. When the tooth socket is not thoroughly debrided, along with incomplete removal of the periodontal ligament, the bone that forms can be incomplete and contribute to trapped pockets of bacteria. There have been many terms to discuss this entity over the years, but the more common words are jawbone osteonecrosis and NICO (Neuralgia-inducing Cavitational Osteonecrosis), or simply "cavitations."

It is essential to understand that cavitations can occur in any bone in the body and that each term has its distinctions. It just happens that cavitations occur in more than half of the sites where teeth are missing. Cavitations, or voids in the bone, can only be produced when blood flow is diminished. Many systemic factors affect blood flow, as well as surgical techniques. Diagnosing cavitations is still tricky as they are not commonly illuminated on 2D radiographs. Even on 3D radiographs, they are not easily detected.

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The most common method of diagnosis has been to evaluate the bone of a CBCT Scan using the HU (Hounsfield) scale. However, other methods are being investigated, such as Acupuncture Meridien Assessment. This method, in particular, is promising in diagnosing dental infections in the jawbone that can contribute to systemic disease. However, there are many more diagnostics that are not available in the United States.

Once the lesion is identified, methods are available to treat the condition. The most common practice is surgical access with the removal of the affected tissue. Some surgical techniques include using a piezo surgical unit to safely navigate the potential nerve and vascular bundles, ozone therapy, and placement of PRF (platelet-rich fibrin). In addition, many clinicians provide pre and postoperative nutrient, diet, and lifestyle recommendations for optimal healing.

Lifestyle support is an exciting field investigated for years by authors such as Lechner, Bouquot, and Boyd Haley. However, mainstream dental and medicine has not embraced it. A stunning recent case study discussed the links of dentistry to chronic autoimmune diseases.²⁰⁷ The patient suffered from neurodermatitis, with no resolution after seven years of conventional treatment. The condition greatly affected her quality of life. The authors solved the problem using ultrasound, X-ray, and immunological and toxicological diagnostics to find and correct hidden oral and maxillofacial infections.

The results of the extensive testing showed medical indications for the surgical intervention of the sites, including four root-canaled teeth, four areas of cavitations, and the removal of two titanium implants. In addition, analyses were done from the lesions in the cavitation sites, showing a 14-fold expression of RANTES/CCL5, a pro-inflammatory marker. The patient's health returned upon installing seven ceramic implants. Her results are astounding, with her dermatologic lesions dramatically improved. This study is an excellent indication of the possible diagnostic methods available to evaluate oral cavity toxicity. Hopefully, these modalities will be available to clinicians sooner rather than later.

We must discuss periodontal disease's role when discussing dentistry and chronic infections. Periodontal disease, or gum disease, is an inflammatory condition that destroys the bone and soft tissue structures that hold our teeth firmly in place. Again, many factors increase the prevalence of periodontal disease, and more than 50 percent of Americans have this condition.

For decades now, thousands of studies have corroborated the connection of inflammation in the mouth to systemic conditions. These conditions can range from stroke, heart attack, dementia, Alzheimer's disease, cancer, lung disease, diabetes, pre-term low birth weight babies, rheumatoid arthritis, glaucoma,²⁰⁸ and COVID-19.²⁰⁹

In 2014, Bale and Doneen wrote the book titled "Beat the Heart Attack Gene." This book is an essential bridge between medical and dental professionals. They

published a paper in 2017 titled "High-Risk periodontal pathogens contribute to the pathogenesis of atherosclerosis," which explains that periodontal bacteria are the contributing factor to atherosclerosis, which is the inflammatory cause of heart attacks. This group offers an objective test for the dental professional, the OralDNA test. This saliva test evaluates the presence of several high, moderate, and low-risk pathogens in the mouth, gives appropriate treatment protocols, and relates how these bacteria affect a systemic disease. It is a valuable diagnostic tool in any office to determine the presence of pathogens that cause gum disease.

I see many patients with heart attacks whose physicians didn't know why they occurred. The Oral DNA test can be very illuminating. This is one of many tools useful for diagnosis. Other simple methods that any clinician can employ are:

- obtaining a hs-CRP level to determine the levels of inflammation;
- evaluating HbA1c to determine their blood sugar control;
- having their Vitamin D levels evaluated, and of course;
- referring to a specialist in gum disease for diagnosis.

There are many more relevant diagnostic markers than those listed here. The hope is that the markers will soon become the standard of care.

What can we do as dentists to improve? As Dr. Williams notes in his book, "A Visit to the Dentist, dental problems are often the result of nutritional deficiencies. Our first goal is prevention starts at home. No amount of brushing and flossing will mitigate the effects of a poor Western diet unless you have some fantastic genetics. As Weston A. Price realized, our diets are sorely lacking in fat-soluble vitamins (A, D, E, K). Eating unadulterated, organic, grass-fed, antibiotic-free, pesticide-free, non-processed foods is healing to your whole body and oral cavity. Removing inflammatory foods from your diet, such as gluten and sugar, also improves oral health.

For many, the thought of revamping their diet is daunting, but it is undoubtedly the key to a healthy life. Try to abide by the 80/20 rule by eating more nutritious foods 80 percent of the time and being laxer the rest of the time.

I would also like to see more applications of appropriate materials. Patients may be more open to this information, which is invaluable to give to your dentist as they get sicker and sicker. In the future, I hope that more reproducible, diagnostic, and objective methods for evaluating failing restorations and root canals will be available to the medical and dental communities. In addition, standardizing updated protocols will decrease the medicolegal worries of some dentists when treating these conditions. Until then, I would like to see more diagnoses of these conditions by simply evaluating clinically, referring to the appropriate dental professional, educating the patient, and taking suitable radiographs and CBCT scans.

And lastly, it is my wish, after 20 years in practice, that more of the medical community will accept the role of oral health and its effect on systemic disease and work with dentists in their community. There is more than enough evidence for this to be the standard of care. I am thankful to work with clinicians and medical advisers such as Dr. Lewis, who understand the role of dental disease in systemic health and educate their patients on these processes.

From a Biological Dentist to You

Dr. Lokensgard is a well-respected biological dentist and naturopath. He has written a book titled, "Matter of the Mouth." He has permitted me to include excerpts from his book in this chapter. Dr. Thom, as he is known, exemplifies what dentistry should be. If you can afford to do so, you should always see a biological dentist instead of the standard dentists who just receive training through the standards set by the American Dental Association.

Biological Dentistry, also known in some circles as holistic dentistry, is the equivalent of functional medicine of the mouth. Biological dentistry aims to get to the causes of oral health issues. Bio-compatible, functional, integrative, bio-mimetic, or natural dentistry are alternative terms for biological dentistry. However, these names are synonymous and interchangeable.

Biological Dentistry considers the following:

- Identify infections of the teeth, face, bone, glands, soft tissues, and jaw.
- Understand heavy metal toxicity, its physiological effects, and how to remove them properly.
- Appreciating what is occurring in the mouth below the gum line is far more important than above the gum line and using advanced measurement techniques beyond two-dimensional X-rays.
- Implement proper organ meridian identification and teeth-organ connections.
- Help people overcome sleep apnea and sinus issues by dealing with oral pathogens
- Choose the best biocompatible and non-toxic replacement dental materials.
- Understand the oral inflammatory connection to chronic degenerative disease and educate patients on this subject.
- Utilize applicable oral inflammatory disease biomarkers (Oral-DNA testing) and blood testing for innate immune responses (white blood cell counts and C reactive protein).
- Understand and communicate the role of proper nutrients in oral and systemic degenerative diseases.
- Explain the oral and cardiovascular inflammatory connection.
- Know the functional orthodontic-temporomandibular disorders (TMDs). These are a group of more than 30 conditions that cause pain and

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dysfunction in the jaw joint and muscles that control jaw movement. "TMDs" refers to the disorders, and "TMJ" refers to the temporomandibular joint.

- Identify osteoporosis and explain how oral and gingival-periodontal health plays a role in this disease
- Understand pH, including salivary, GI health, and its connection to immune health.
- Utilize natural methods to maintain oral systemic and gut health.
- Treat dental infections with platelet-rich plasma (PRP), ozone, and other necessary agents to mitigate any systemic infiltration of these organisms.
- Implement the best traditional techniques, including routine cleaning and scaling, regularly.
- Help patients implement home preventative dentistry measures not embraced by the ADA and traditional dentists.
- Discourage fluoride, which is toxic to bones and other tissues and may impact the thyroid and other physiological functions.
- Educate patients on cavitations, who is at risk, and what can be done about them if found.
- Give practical advice on saving or removing teeth instead of recommending root canals.

Compare this thorough but incomplete list of considerations of a biological dentist to what you receive during a traditional dental visit.

- Affect routine cleaning.
- Obtain 2-dimensional x-rays that only identify late-stage changes.
- Recommend root canals.
- Often remove mercury without appropriate safeguards from exposure.
- Give samples of fluoride-containing toothpaste.
- Note recession and cavities.
- Prescribe or recommend toothpaste with higher fluoride levels compared to over-the-counter products.
- Give little advice on gingivitis or periodontal disease at its early stages.

According to Dr. Thom, "it is of utmost importance for everyone to understand that you are neither healthy nor sick. Instead, you reside somewhere on the oral health-disease continuum. And, oral health is whole body health."

Here is Dr. Thom's protocol for home oral care, which he calls "how to clean your teeth naturally."

Perform oil pulling. This involves placing an oil like coconut or sesame in your mouth and swishing and "pulling" the oil through your teeth with suction for 10 minutes. Do this a couple of times each week. The purpose is to remove the biofilm that builds up as tartar. The biofilm is the housing project for bacteria in

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the mouth. It starts as a slimy material that the oil can "pull" or dissolve and remove from your mouth. It does not form instantly, so oil pulling need not be done daily.

Rise your mouth with water frequently. You may not be able to brush after every time you eat, but you can rinse your mouth with water. I highly recommend that you do this. Swish, then spit! This dilutes the oral acids that result from any food with sugars.

Drink a 1-full glass of pure water with a small amount of sea salt daily with freshly squeezed lemon juice. It helps add back the minerals. Do this three times daily. I recommend drinking 4 ounces of mineralized water every hour. Your system can handle the smaller amounts more efficiently.

Use a SONICARE toothbrush. Make your own toothpaste with baking soda, coconut oil, and peppermint oil. Some people find salt very stimulating to the gums, so dipping a wet toothbrush in pickling salt and then brushing is something to consider a couple of times each week.

Gum and sugar. If you chew gum or must eat sugar, use Xylitol, but even then, do this sparingly. Chewing gum stimulates the production of digestive juices and can make you hungry even when you are fully nourished.

Anti-inflammatory food. Consume sufficient anti-inflammatory foods, with healthy fats topping that list. Cod liver oil is an excellent option. It is a fish oil with fat-soluble nutrients like vitamin K, which help make calcium available for your teeth.

Mineral support. Take in boron and silicon compounds that support the parathyroid hormone and thus calcium balance. Your teeth are primarily calcium.

Neutralize mouth acids. I have a crazy friend who wrote this book that brushes with pure lye soap. As odd as that seems, the soap helps remove biofilms, and it is also alkaline, like baking soda, so it is a very inexpensive alternative to toothpaste. If you make toothpaste at home, add a touch of essential oil, mainly clove and thieves oils. Of course, never use traditional toothpaste, especially those with fluoride. They provide no value other than to get you to brush.

Floss. Floss with water and string/tape daily. Avoid using aggressive anti-pathogenic additives like peroxide. If you have a bad case of gingivitis, using peroxide rarely may help, but it also destroys the oral biofilm necessary for healing. Adding a bit of iodine or salt to the water flosser tank will be adequate to reduce bacteria. Do this on a weekly rather than a daily basis.

Oral microbiome. Look into oral microbiota products. New ones are coming on the market and likely will improve your oral hygiene. But, of course, the best antibiotics are actually probiotics.

Test for pathogens. Testing is crucial because many people have a simmering oral infection for years before it becomes noticeable in the mouth. However, even when your regular dentist says your mouth is "perfect," you may be aware of mouth-related problems systemically but not make the connection.

Sleep Apnea and Oral Issues

Do you have a CPAP machine deficiency? CPAP stands for continuous positive airway pressure therapy. Could it be that somewhere along our evolutionary development, we lost the attachment of this machine to our heads? Of course, this is nonsense. My brother wears his CPAP device religiously. He is a veteran and uses anything the VA doctors give him without question. Might disruptive sleep be due to a sinus infection from the mouth?

According to Orthodontics of Texas, "People with obstructive sleep apnea (OSA) are more likely to struggle with moderate to severe periodontitis (gum disease). In addition, they are even more likely to develop temporomandibular joint disorders (TMD)." In my opinion, this statement is the cart before the horse. People first have periodontal disease leading to TMD disorder and then develop OSA.

Dr. Thomas Lokensgard, in his upcoming book titled "Matters of the Mouth," explains OSA and other mouth and general health issues that result from improperly formed bone structures.

"One of the most neglected topics in dentistry today is oral-facial myology and oral-facial growth. I say this because many complications can and do occur later in life if the face is not fully formed or grows improperly early on in a child's developmental years.

Facial orthopedics can improve functional conditions, promote a more favorable jaw relationship, guide the development of the dentition, and improve the position of misaligned teeth. This allows for better placement of the various structures related to the mouth. For example, suppose the jaws are too narrow, and the tongue cannot reach the palate due to a tongue tie. In that case, the Maxilla (upper jaw) will not develop to its proper size, and the Mandible (lower jaw) will drop to the back of the throat, causing pharyngeal airway obstruction and decreased oxygen consumption, plus fatigue. This is just the beginning of a long list of potential problems.

Next, during the day, the tongue begins to protrude through the upper and lower teeth contributing to potential speech issues, a narrower and shorter lower face height, extremely crowded teeth, plus compressed retruded condyles. Finally, at night, the tongue again flops back into the throat, contributing to snoring, obstructed sleep apnea, and continued mouth-breathing, which perpetuates hypoxia (lack of oxygen), fatigue, and a decrease in overall metabolism.

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It gets worse. The sinuses do not develop well because of improper airflow and critical air exchange that does not cool off the sinuses and impinges on the pineal gland and the pituitary gland, which are absolutely essential for whole-body growth and development. Get the picture? So, here's the deal. Breastfeed your baby. It helps them to develop their jaws, become nose-breathers, and grow to their God-given potential.

These methods often solve CPAP deficiency, but you must start a pre-birth prevention program. The best you can do after that is to consume high-nutrient-dense foods to support the health of the bones and your immune system. Is your regular dentist telling you about this? I suggest you go to a biological dentist. Sure, you can go to a regular dentist for cleanings. But, for advice pertaining to the mouth, get that from a biological dentist."

We were at the Truth About Cancer Live in 2021 in Nashville. There were about 5,000 attendees. A group of about a dozen of us was standing outside the main lecture hall, discussing. I asked a question of the group that included two biological dentists, John Grill and Thom Lokensgard. The question was, "what is the biggest contributor to premature aging, at least in America?" One person suggested the use of statin drugs. That is near the top, for sure. Another person said the loss of a diverse microbiome. I had no choice but to agree that this is the #1 issue. But then I offered a one-word reason "dentists." The two biological dentists shook their heads in agreement. So at least we agreed that dentists might be the #2 cause of premature aging.

"Weston A. Price, DDS" is the blog title on the Weston A. Price Foundation website.²¹⁰

"Dr. Weston A. Price (1870-1948), a Cleveland dentist, has been called the "Isaac Newton of Nutrition." In his search for the causes of dental decay and physical degeneration that he observed in his dental practice, he turned from test tubes and microscopes to unstudied evidence among human beings. Dr. Price sought the factors responsible for fine teeth among those who had them - the isolated "primitives."

The world became his laboratory. As he traveled, his findings led him to believe that dental caries and deformed dental arches resulting in crowded, crooked teeth and unattractive appearance were merely a sign of physical degeneration, resulting from what he had suspected-nutritional deficiencies.

Price traveled the world to study isolated human groups, including sequestered villages in Switzerland, Gaelic communities in the Outer Hebrides, Eskimos, and Indians of North America, Melanesian and Polynesian South Sea Islanders, African tribes, Australian Aborigines, New Zealand Maori and the Indians of South America. Wherever he went, Dr. Price found that beautiful straight teeth, freedom from decay, stalwart bodies, resistance to disease, and fine characters

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were typical of native peoples on their traditional diets, rich in essential food factors."

Another Weston A. Price blog is titled "From Attention Deficit to Sleep Apnea."²¹¹

Virtually everyone in the Weston A. Price Foundation is well aware of the incomparable anthropological research conducted by Dr. Price. In the 1930s, this dedicated holistic dental physician spent his summers studying fourteen traditional cultures worldwide. In his subsequent book, "Nutrition and Physical Degeneration," Price wrote that none of these native peoples were vegetarian, but in every case, consumed some combination of meat and organ meats, fish, shellfish, eggs, and raw milk, cheese, and butter.

He further found that these groups, not exposed to the refined and toxic foods of modern civilization, displayed three exceptionally healthy characteristics:

- First, they had almost no cavities.
- They had normal facial and dental bone development with room for all thirty-two teeth.
- They were observed to be very "happy and contented" with "a high sense of humor" and often displayed "superior intelligence."

Contrast these signs of optimal mental and physical health with today:

- Dental cavities are commonplace and even considered by the general populace to be an unpleasant but inevitable aspect of growing up.
- Similarly, extraction of the wisdom teeth (third molars) is now a normal rite of passage for nearly all teens and young adults since almost no one has the craniofacial and dental bone development required to house all thirty-two teeth.
- Finally, the enormous percentages of children and adults prescribed SSRI drugs, such as Prozac, Paxil, and Zoloft, clearly demonstrate that anxiety and depression in this country have become truly epidemic. Additionally, the growing number of children prescribed Adderall, Concerta, and other medications for ADD (attention deficit disorder), ADHD (attention deficit hyperactivity disorder), and additional learning and behavioral disorders vividly illustrates the serious challenges younger generations are currently experiencing both psychologically and intellectually.

Mild to major respiratory and breathing problems are also classic symptoms of malocclusions. It is no mystery that crooked and crowded teeth (malocclusions) and sleep apnea have both continued to rise at an unprecedented pace. This nightly respiratory distress and resulting insomnia narrow the "V-shaped" palate, which pushes up on the floor of the nasal cavity, reducing one's breathing efficiency. This forces many children (and adults) to open their mouths at night to receive more oxygen.

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Raymond Silkman, a holistic dental physician and Price Foundation contributor, describes this mouth-breathing habit as a chronic distress signal to the autonomic nervous system. Dr. Silkman found that these mouth-breathing patients live with permanent tension and chronically experience a sense of being on "high alert" from their amped-up sympathetic nervous systems.²¹² The resulting mild to major systemic anoxia (lack of oxygen) harms every cell in the body. Chronic anxiety, certain types of headaches, hypertension, reduced heart rate (bradycardia), blood-clotting dysregulation, enuresis (bedwetting), and chronic nose, ear, and sinus infections are consequences of this process. According to Dr. Silkman,

"Dr. Weston A. Price, the quintessential biological dental physician, not only specialized in nutrition and treating dental foci (such as failed root canals) but was a trailblazer in functional orthodontics. In another dramatic functional orthodontic case, Price widened the narrow upper arch of a Down's Syndrome teen approximately 1/2 inch with a palatal expansion rod device located between his upper teeth. In so doing, the new maxillary bone filled in rapidly. Later, an installed fixed bridge with two additional teeth attached solved the problem."²¹³

Once again, the results from the palate expansion on a sixteen-year-old were striking. This patient had an I.Q. of a four-year-old. The patient was physically and mentally impaired and played with blocks incessantly. However, after six months of palate expansion, he could go to the grocery store and bring back correct change to his mother, change trains and make transfers on streetcars accurately and safely, and read children's stories and newspaper headlines.

This teen's physical appearance also dramatically transformed. He grew three inches in four months, developed whiskers, and his genitals enhanced from those of a child to a man. These hormonal maturation changes were the direct result of the stimulation of the pituitary gland through the expansion of the sella turcica - the saddle-shaped depression in the sphenoid cranial bone that houses the pituitary. Down's syndrome causes the failure of the development of the middle third of the face and the pituitary. Finally, this teen's severe sleep apnea was relieved when the expansion device opened up his completely occluded left nostril so he could breathe properly."

Fluoride

The fluoride issue is about health freedom and not dental caries. Communities that add fluorine compounds to water leave their citizens with no or little choice. In many cases, people are unaware that synthetic fluorine compounds are added to their tap water. Most people know chlorine is present to sanitize the water in one form or another. Many fluoride health freedom issues confront us. You do have choices in some instances.

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- Fluoride toothpaste: You do have a choice.
- Fluoride in water: If you cannot afford expensive removal systems or bottled water, you have no choice but to take this toxin at unnaturally high levels.
- Dentists often encourage fluoride as the only option to reduce dental decay, even though it is NOT the root cause of the process.

This does NOT look like health freedom to me.

Even if adding fluoride to water is safe, it is still a failure. Water fluoridation is most likely not sufficiently concentrated to impact tooth enamel but is enough to harm health. Figure 6.5 shows the rates of tooth decay in countries with and without fluoridation in water.

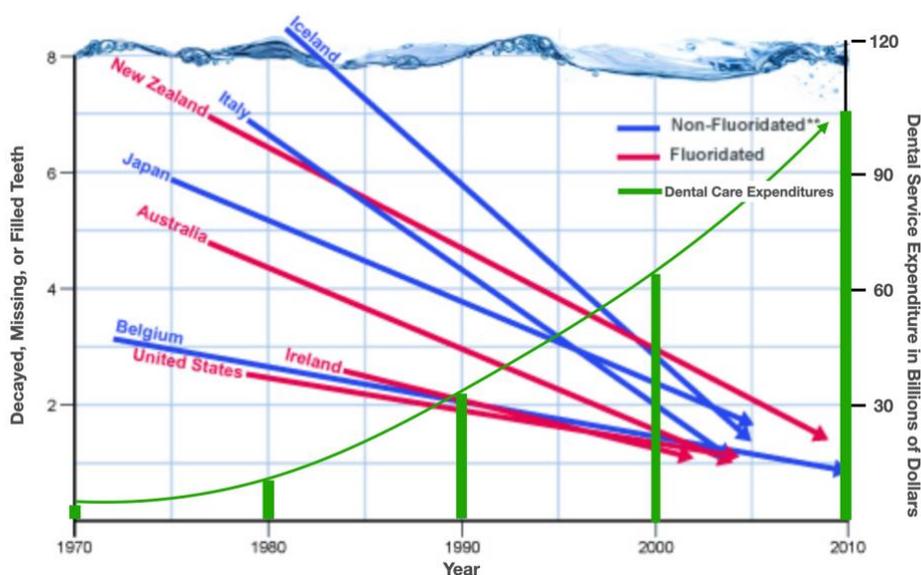


Figure 6.5 The left axis is the rate of dental decay measured in countries with and without water fluoridation. The right axis is the expenditure for dental care over the same period. The vertical green bars emphasize dental spending in the United States during specific years.

Fluoride toothpaste was introduced in the late 1950s. Many sources attribute the dramatic reduction in cavities in the 1970s to these pastes and fluoride compounds in the water. However, the dramatic upswing in dentists, as reflected by dental spending, had no impact on dental health, according to the fluoride zealots. From figure 6.5, these conclusions emerge.

- Water fluoridation has no impact on tooth decay.
- Fluoride in toothpaste may impact tooth decay.
- Dental visits impact tooth decay.

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The fluoride advocates fluoride is predominantly responsible for reducing cavities. Why are we spending so much on dental care if that is the case? Do we need to go to the dentist? Do we need to brush our teeth, or can we just let the fluoridated water seep into the enamel and never have a cavity again?

If you want to live a long healthy life, enamel health is the least of your concerns. Aging people are often referred to as "long in the tooth." This is an upside-down explanation as the process is becoming "short in the gums." What does fluoride do for gum health other than nothing? "Short in the gums" means the individual has periodontal disease, not cavities.

I never join a society because they all have hidden agendas. I would like to be a member of the American Chemical Society (ACS), but I cannot align myself with any misinformation. The ACS should be the authority on fluoride, but they fall short and promote chemicals, including fluoride. This is not a surprise. They are the American Chemical Society. An article from the ACS titled "New evidence on how fluoride fights tooth decay"²¹⁴ promotes the use of synthetic fluoride.

Karin Jacobs and colleagues explain, "despite a half-century of scientific research, controversy still exists over exactly how fluoride compounds reduce the risk of tooth decay. That research established long ago that fluoride helps to harden the enamel coating that protects teeth from the acid produced by decay-causing bacteria. Newer studies have already found that fluoride penetrates and hardens a much thinner layer of enamel than previously believed, lending credence to other theories about how fluoride works."

The report describes new evidence that fluoride also impacts the adhesion force of bacteria that stick to the teeth and produce the acid that causes cavities. In addition, the experiments revealed that fluoride reduces the ability of decay-causing bacteria to adhere. So, in theory, washing away the bacteria with saliva, brushing, and other activities are easier.

The report describes new evidence that fluoride also impacts the adhesion force of bacteria that stick to the teeth and produce the acid that causes cavities. Do we really need to put an antibiotic in the water and our toothpaste? Polluting our water is completely unnecessary. There are much better ways to protect our teeth and gums without spreading an aggressive chemical throughout our environment.

Dissect the language from the ACS publication. The emphasis of the article is on fluoride. However, the cause stated is bacteria. Do you really think fluoride is the proper treatment for oral bacteria? The solution provided by my chemistry colleagues, fluoride use, completely missed the root cause solution - treating bacteria.

The ACS indicates that fluoride reduces the impact of bacteria on the teeth. Bacteria is a crucial issue and opens the door to eliminating fluoride use. The oral protocol presented by Dr. Thom Lokensgard above is designed to "reduce the impact of bacteria" without fluoride.

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Most believe fluoride can harden the enamel because it is a small molecule that creates strong bonds. This is reasonable, but why, after 50 years, is this not a proven mechanism? However, something else hardens boney tissue. It is a drug called Fosamax. Figure 6.6 shows what happens when bones are chemically altered with an unnatural chemical.



Figure 6.6. A common side effect from the use of Fosamax is a clean fracture that occurs, in many cases, upon minimal trauma.

What does Fosamax do? It makes a flexible bone more brittle. What does fluoride do? It makes your teeth more brittle.

Bad deal.

Fluoride is ubiquitously present throughout the world. It is released from minerals, magmatic gas, and industrial processing and disperses in the atmosphere and water. Exposure to fluoride in the part per million (PPM) range results in broad human toxicity. This includes oxidative stress, organelle damage, apoptosis in single cells, and skeletal and soft tissue damage in multicellular organisms. Fluoride toxicity is attributed to four mechanisms: inhibition of proteins, organelle disruption, altered pH, and electrolyte imbalance.

The altered electrolyte balance is not well studied or at least not well described in the scientific or medical literature. However, due to its strong affinity for electrons, fluoride will out-compete other minerals leading to electrolyte imbalances. Electrolytes drive the electricity in our bodies by facilitating active transport - the process of getting nutrients into and out of cells. Fluoride, chemically similar to iodide, is reported to impact thyroid health. Thyroid disease is common in modern society. Coincidence?

Fluoride is a naturally occurring substance. It is found in nature at low levels, so it probably benefits soils, organisms, plants, and animals. At levels greater than found in nature, but even at low levels in fluoridation, it impacts health. Sixty percent of U.S. adults have at least one chronic condition. Might fluoride, at artificially augmented levels, be a contributor? The dose makes the poison. These

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are the kinds of outcomes that are hard to prove or disprove, even in well-designed clinical trials. Why? Chronic diseases develop over 20+ years, and clinical trials last only five years.

Dr. Zev Zelenko was a champion of COVID-19 early treatment. He set forth three (3) criteria for using any treatment. Here are the three ways they apply fluoride in toothpaste and drinking water.

Is it safe? The dose makes the poison, and fluoride is an aggressive and toxic substance even at low doses. The "jury is still out" concerning fluoride at the levels used in dentistry and how the available data points to potential harm.

Is it effective? The data does not support effectiveness. Oral pathogens constitute the actual oral health risk, not the structure of teeth.

Is it necessary? Adding fluoride through any means is entirely unnecessary. Science has advanced substantially since fluoride was first introduced in the 1950s and subsequently supported by the American Dental Association. My 2018 Camry Hybrid is superior compared to my grandmother's 1957 Chevy. The same is true of biological dental care devoid of fluoride.

Functional Periodontist Speaks Out on Fluoride

Dr. Patricia Berube weighs in on fluoride. As a functional periodontist, what she sees clinically matters.

"I am hard-pressed to find anyone who does not equate dentistry with fluoride. At the beginning days of practice, when someone would inquire about what toothpaste to use, my standard response was, "anything that the ADA recommends." How have times changed? Let me explain. In the past, I did not question what was taught. I never looked at ingredients in food or hygiene products. Fast forward several years, and my opinion has changed 180 degrees. Is it because of the skull and crossbones present on a tube of toothpaste? Is it the hundreds of cases of fluorosis that I have seen on permanent teeth?

Even when I worked for a pediatric dentist before dental school, the number of fluoride-affected teeth we saw was shocking. What I am talking about is the whitish lesions on adult teeth. Depending on the severity, these are permanent and can only be remedied by placing veneers or crowns, which involves breaking down precious tooth structures. Some teeth are so affected that they have turned a brownish color. If you research what fluorosis looks like, you will see it is very disconcerting. People say this is purely aesthetic but is it? Let's discuss some facts.

What is fluoride? According to CDC.gov, fluoride is a mineral that occurs naturally and is released from rocks into the soil, water, and air. Almost all water contains some fluoride, but usually not enough to prevent tooth decay.

Is it an essential nutrient? No. The FDA determines whether or not any substance is essential. Fluoride is not an essential nutrient because no deficiency state related

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to a health problem could be found. In animal studies, the least exposed animals had the fewest cancers and the least dental fluorosis. The Federal Register in 1979 stated that "the FDA removed all references to fluoride as a nutrient or probable nutrient." Fluoride, as an additive, has never been approved as a drug suitable for anyone. In other guidelines, the government has expressly excluded young children under age three from exposure.

Fluoride is an unapproved drug for which the FDA has no evidence of safety or effectiveness. As a result, they have issued multiple regulatory letters demanding companies stop manufacturing vitamins and systemic tablets or drops with fluoride.²¹⁵

I had no idea how many products contained fluoride until I started researching and learning about what I had been recommending all these years. Fluoride is present in:

- community water fluoridation;
- dental products such as dental cement, fillings, gels, and varnishes;
- floss, mouthwash and toothpaste, soft drinks, juices, and alcoholic beverages;
- pharmaceutical drugs;
- chemicals in carpets;
- cleaners;
- clothing;
- cookware;
- food packaging, paints, paper, and related products.

There are also products made from hydrogen fluoride, which include:

- aluminum;
- electrical components;
- fluorescent light bulbs;
- herbicides;
- high-octane gasoline;
- plastics;
- refrigerants, and
- etched metal and glass (such as in some electronic devices).

What levels of fluoride in water are deemed "safe"? For decades, there has been disagreement on fluoride's maximum contaminant level (MCL). It began at a low level and then increased to 4 mg/L (ppm) as determined by the EPA. Due to lawsuits against the EPA to decrease the MCL, they enlisted the National Research Council (NRC) to evaluate fluoride risk. A report released in 2006 by the NRC noted that the EPA's maximum contaminant level goal for fluoride should be lowered. Considering that a level determined to be too high is four ppm,

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fluoride is naturally present in soil and water, and many municipal water systems add one ppm, could the dose in your tap water be over a safe level?

Many of us assume fluoride added to water is pharmaceutically pure. This could NOT be farther from the truth. It is very troubling to find out that the fluoride in our drinking water is almost exclusively raw industrial pollution from the Florida Phosphate Industry. It is a waste scrubbed from the smokestacks, trucked in tankers, and dumped into reservoirs.

Many websites and research papers state fluoride decrease caries by 25 percent to 40 percent. But the facts just don't support this. These percentages are in relative statistics that are meaningless to your health. Note how the decrease in caries does not depend upon water fluoridation but corresponds well with dental care expenditures (Figure 6.6). A Cochrane review, a true evidence-based and scientifically valid assessment of water fluoridation evaluated in blinded studies, has not found a statistically significant difference in permanent tooth decay regardless of drinking water with fluoride.

Even if fluoride did reduce dental caries, what does it do to the rest of your body at the dose provided in municipal water? Why would fluoride be dosed by putting it into your body instead of directly on your teeth?

A reasonable body of research shows that people with dental fluorosis also have skeletal fluorosis. This is a condition that is a "chronic metabolic bone and joint disease caused by ingesting large amounts of fluoride either through water or from foods of endemic areas."²¹⁶ The authors of this peer-reviewed report indicate, "fluoride is a cumulative toxin that affects the homeostasis of bone mineral metabolism. The total quantity of ingested fluoride is the single most important factor determining the disease's clinical course, characterized by the immobilization of joints of the axial skeleton and the major joints of the extremities. A combination of osteosclerosis, osteomalacia, and osteoporosis of varying degrees, as well as exostosis formation, characterizes the bone lesions." A subsequent study by the National Academy of Sciences in 2006 identified an increased risk of bone and hip fractures from fluoride exposure.²¹⁷

Other systemic conditions associated with fluoride include:

- arthritis;
- behavioral problems;
- cardiovascular diseases;
- digestive problems;
- endocrine irregularities;
- immune dysfunction;
- renal system dysfunction;
- dermatological problems;
- diabetes;

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- learning difficulties
- skeletal fluorosis; and
- thyroid deficiency.

A quote from a 2011 literature review states: "If we were to consider only fluoride's affinity for calcium, we would understand fluoride's far-reaching ability to cause damage to cells, organs, glands, and tissues."²¹⁸ A recent study from Canada in a journal called *Nutrients* found that pregnant women with low iodine levels and elevated fluoride had boys who suffered an average IQ loss that was 58 percent greater than the already significant IQ loss from high fluoride alone.²¹⁹ This is not the first study to look at the effects of fluoride on IQ. [Thefluoridealert.org](http://thefluoridealert.org) cites 64 studies that link fluoride with reduced IQ in children.

Another item we can add to the list is the effects of fluoride on our bodies on the pineal gland. Fluoride is known to calcify the pineal gland. This gland produces melatonin. Melatonin is the hormone that regulates the sleep-wake cycle. This study concluded that "fluoride exposure may contribute to changes in sleep cycle regulation and sleep behaviors among older adolescents in the US."²²⁰

Do you know anyone with sleep problems?

Again, as a functional periodontist, I evaluate and treat severe oral issues a dentist does not. Here is a case study of a patient I have seen for over a decade. When I began seeing her, she was obese with a thyroid condition. She was referred to a regular dentist to manage her periodontal disease and was placed on high-dose fluoride to control caries. This is still common practice in most dental offices as the primary way to help prevent dental cavities. Unfortunately, she was diagnosed with an autoimmune disorder, and her health deteriorated.

I saw her and eliminated the fluoride treatment. Is it possible that fluoride overloaded her body and thyroid, affecting her melatonin levels, thus, her sleep, which impacted her health in general? Her health is improving, but it takes time to remove fluoride because it binds very strongly to everything. Since the thyroid is an energy hormone-producing gland dependent upon iodine, supplementation may help people, like this lady, with the multifactorial disease.

Every substance has the potential to be beneficial, cause no effect, or be toxic. Therefore, the expression "the dose makes the poison" applies. Also, in nature, everything responds to the bell curve. This means the response is log-linear. Figure 6.6 shows my estimation of the dose/toxicity relationship for fluoride. Adding fluoride to our water supply increases the fluoride concentration to unsafe levels.

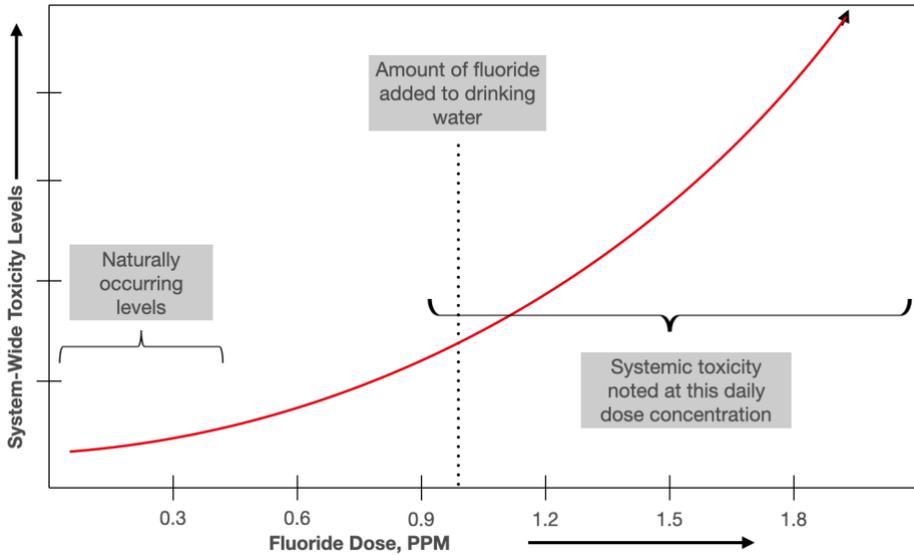


Figure 6.6. Estimated toxic response to fluoride based on concentration. Fluoride is added to municipal water supplies at 1 PPM. The baseline fluoride concentration is unknown in any water supply. Therefore, the total amount of fluoride in the water is unknown, hence the potential toxicity.

If fluoride is not an essential nutrient, nor even deemed safe to use, why is it added to the water? Again, I believe this quest began with the goal of decreasing caries in children while saving money on dental care. But the reality is it turned into something different. At this point, I don't recommend it in my office. Even when I worked in a pediatric dental office, I concluded that I'd instead fill my child's cavity than subject them to the unsightly lesions of toxic fluoride and the potential systemic effects. Knowing what I know now, the data supports my assertion in many more ways that are more important.

Fluoride is a very sticky substance chemically. This is not a guess; it is based on the periodic table of elements where fluorine is the most electronegative. This has health consequences, particularly in children. The fluoride sticks firmly to saliva, which is then swallowed. On average, a person swallows well over a quart of saliva daily. If your child brushes with fluoride toothpaste, even if they rinse, how much fluoride are they ingesting? An adult may be taking in the same amount of fluoride daily. However, if the adult weighs 200 pounds and the child weighs 40 pounds, the toxicity impact on the child will be at least 500% greater. In this context, please re-read the systemic side effects of excess fluoride.

Considering that many children now exceed the recommended daily fluoride intake from toothpaste alone, it is just not something I'm willing to take a chance on. Caries prevention involves maximizing Vitamin D levels, decreasing sugar consumption, improving the diet, and providing effective oral care, including

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maintenance visits. Ninety-seven percent of European nations have rejected fluoride in the water supply. The United States lags behind. The Fluoride Action Network is a fantastic group to join. Another way you can help is by investigating the contents of your local water and by making your feelings known to your local water boards. I was so happy that our water does not add any chemical forms of fluoride and only includes the elements found in nature. But you don't know until you check.

Speaking of checking, I mentioned the role of Vitamin D deficiency and caries. I have two children, and both have similar diets, yet one had three cavities when he was very young. I was perplexed, especially considering you could argue that he ate healthier foods and would down a salad with no complaints. Years ago, I obtained a genetic test and noted that he had an SNP called VDR, a Vitamin D receptor defect. I began supplementing more Vitamin D. I never put two and two together until the lockdown. I was researching the role of Vitamin D deficiency and dental implant failures. It turns out that Vitamin D deficiency is related to many oral health disorders. In Botelho's review,²²¹ they note that Vitamin D deficiency can induce defective tooth mineralization. Low vitamin D is associated with periodontitis and gingival inflammation, failure of procedures, certain oral cancers, and osteonecrosis.²²¹

"This simple "vitamin" has changed how I practice. I believe obtaining optimal Vitamin D levels is paramount for optimal oral health."

Be Well - Patricia Berube, DMD

The aggressive nature of fluoride and its overall lack of benefit to the key aspects of proper oral care make fluoridation conspiracy theories worth considering. Ignorant people suggested putting statin drugs in our water supply. The only thing that should be in our water is water.

Consider reading an article by Kilmer S. McCully, M.D. He is a Harvard medical doctor with the utmost integrity. In the 1960s, he knew the cholesterol theory of cardiovascular disease was incorrect. He demonstrated that elevated homocysteine was deleterious to vessel health. He was at Harvard at the time. What did the evil empire do? Harvard fired and blacklisted him. He had to travel two hours to find work until Harvard reinstated him 30 years later. Dr. McCully has written hundreds of papers, mostly discussing disease mechanisms. The paper he wrote that includes information on fluoride is titled "Environmental Pollution, Oxidative Stress, and Thioretinaco Ozonide: Effects of Glyphosate, Fluoride and Electromagnetic Fields on Mitochondrial Dysfunction in Carcinogenesis, Atherogenesis, and Aging."²²²

Fluoride Deception

Chris Bryson, the author of "Fluoride Deception," delivers a haunting message that fluoride was not thoroughly studied before it was foisted on the public as a panacea to protect or improve oral health. Bryson reveals that the safety of

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fluoride became a firmly established paradigm based on incomplete knowledge. Due to the COVID era, we have a new understanding of how officials with an agenda define "safe and effective." The American Chemical Society supports fluoridation while explaining that how it works within teeth is unknown. If how it works is unknown, then its safety profile is unknown.

The Ohio State University published a series called "Origins - Current Events in Historical Perspectives. In addition, they published one on fluoride titled "Toxic Treatment: Fluoride's Transformation from Industrial Waste to Public Health Miracle."²²³ It is quite a thorough review of how fluoride wound up in our water. Excerpts from that article are included here.

"While Florida calls itself the Sunshine State, from a geological and economic perspective, it could just as accurately be known as the Phosphate State. The so-called Bone Valley of central Florida contains some of the largest phosphate deposits in the world, which supply global agriculture with one of its most essential commodities, synthetic fertilizer. In the process, the mining industry left behind a scarred landscape denuded of vegetation and pocked with vividly colored waste disposal ponds that one writer described as "beautiful pools of pollution."

Highly toxic hydrogen fluoride and silicon tetrafluoride gases are by-products of fertilizer production. Before the 1970s, these pollutants were vented into the atmosphere and gave central Florida some of the most noxious air pollutions in the country. During the 1960s, however, complaints by farmers and ranchers eventually forced reluctant manufacturers to invest in pollution abatement scrubbers. Unfortunately, these scrubbers converted toxic vapors into fluorosilicic acid (FSA), a dangerous but more containable liquid waste. A hazardous summary fact sheet from the New Jersey department of health is linked to this endnote.²²⁴

The U.S. National Institute for Occupational Safety and Health (OSHA) cautions that FSA, an inorganic fluoride compound, has dire health consequences for any workers that come into contact with it. Breathing its fumes causes severe lung damage or death, and an accidental splash on bare skin will lead to burning and excruciating pain. Fortunately, it can be contained in high-density cross-linked polyethylene storage tanks.

It is in such tanks that fluorosilicic acid has, for the past half-century, been transported from Florida fertilizer factories to water reservoirs throughout the United States. Once there, it is drip fed into drinking water. This is a practice that the American Dental Association and numerous scientists and public health officials describe as "the precise adjustment of the existing naturally occurring fluoride levels in drinking water to an optimal fluoride level for the prevention of dental decay."

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Adding fluoride compounds (mostly FSA and occasionally sodium fluoride) to drinking water is known as community water fluoridation. It has been a mainstay of American public health policy since 1950. It continues to enjoy the support of government health agencies, dentists, and others in the medical and scientific community.

Most of us do not know about the safety of chemical additives in our food. For example, red dye #3 was determined to be a carcinogen. Yet, it took a dozen years after the finding to remove it from our food supply.

"Many are surprised to learn that, unlike the pharmaceutical-grade fluoride in their toothpaste, the fluoride in their water is an untreated industrial waste product that contains trace elements of arsenic and lead. Without the phosphate industry's effluent, water fluoridation would be prohibitively expensive. And without fluoridation, the phosphate industry would be stuck with a costly waste disposal problem.

Only a handful of countries fluoridate their water - such as Australia, Ireland, Singapore, and Brazil, in addition to the United States. Moreover, western European nations have rejected the practice. Nonetheless, dental decay in Western Europe has declined at the same rate as in the United States over the past half-century. In fact, the more one looks at the history of fluoridation, the more it appears to be a relic of the sort of mid-20th century scientific incaution that gave us DDT, thalidomide, and other attempts at "better living through chemistry.

This is not to vilify the early fluoride advocates, who had a legitimate reason to believe that they had found an easy and affordable way to counter a significant public health problem. Unfortunately, the arguments and data used to justify fluoridation in the mid-20th century and the fierce commitment to the practice remains unchanged. Moreover, authorities failed to consider a shifting environmental context that may have rendered it unnecessary or worse.

Dr. Frederick McKay, a dentist, became perplexed by the unsightly tea-colored stains that discolored many of his patient's teeth, a condition he could not find in the dental literature. McKay began calling it "brown stain" and "Colorado stain." Nobody understood why many residents of that particular region suffered from it while those in neighboring counties did not. In the summer of 1909, McKay and some colleagues inspected the mouths of 2,945 Colorado Springs children and discovered that 87.5% suffered from the condition.

Upon further investigation, McKay determined that the Colorado Springs area was not unique. There were pockets of brown stain throughout the country. So McKay began to conduct an informal epidemiological study.

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He examined the local diet, soil conditions, and air quality but eventually decided that the culprit had to be the water.

"The evidence is so conclusive," he wrote in 1927 to the Public Health Service (PHS) in Washington, D.C., "that it is futile to discuss it further from any other standpoint." Despite testing numerous samples, he could not find anything unusual in the local water supply, which was clear, odorless, and agreeable to the taste. Nevertheless, he became increasingly convinced that some undetected trace element in the water was responsible for the dental lesions.

A big step toward solving the mystery of brown stain occurred in 1931 when nervous chemists at the Aluminum Company of America (ALCOA) began to examine the water in Bauxite, Arkansas. The principal ore of aluminum, bauxite, was vital to ALCOA's production process. In 1909, the town's growing population necessitated a new water supply, and ALCOA dug three deep wells to access the ample groundwater. In a few years, children in Bauxite began to be afflicted with brown stains. Initially, this was of no great concern to ALCOA. By the late 1920s, however, the company was fending off charges that its aluminum cookware was slowly poisoning the population.

ALCOA's chief chemist, H. V. Churchill, was concerned that any link between aluminum and brown stain would be a public relations disaster. So, in 1930, he tested Bauxite's water supply using the most advanced spectrographic equipment available at the time. The tests showed that the groundwater had unusually high levels of the element fluorine - 15 parts per million (ppm). As a result, he wrote McKay, "so unexpected in water that a new sample was taken with extreme precautions," but showed the same outcome. Soon after Churchill's tests revealed the presence of fluoride compounds in water, animal experimentation by scientists at the University of Arizona firmly established a causal relationship between fluoride ingestion and stained teeth.

While McKay and Churchill were busy revealing fluoride's undesirable effect on human teeth, a young Danish scientist, Kaj Roholm, was investigating the impact of industrial fluoride on human health. In 1930, a dense layer of polluted fog settled over the Meuse Valley, a heavily industrial area in eastern Belgium, killing sixty people and sickening thousands. After a lengthy and careful investigation, Roholm determined that gaseous fluoride compounds were responsible. Roholm also identified aluminum smelters as emitters of large quantities of fluoride gases.

Just as fluoride's negative image was beginning to crystalize in the minds of scientists and public health officials, however, a countervailing set of ideas started forming. Ironically, it also stemmed from the work of Frederick McKay. As far as McKay could tell, the staining did not

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compromise teeth' strength or physical health. On the contrary, people living in endemic brown-stain regions seemed to have fewer cavities than the general population.

The man who played the major role in transforming fluoride's medical image from tooth disfigurer to a potential prophylactic against dental caries was Trendley H. Dean. A St. Louis dentist who joined the Army Dental Corps in World War I, Dean became a key figure in public health dentistry. In 1930, he was appointed chief scientist of the newly established Dental Research Section of the National Institutes of Health. Then, in 1948 became the first director of the National Institute of Dental Research.

Dental caries was perceived as one of America's most widespread health problems in the early twentieth century. Many dentists and medical scientists were convinced that Americans' diets, particularly their fondness for refined flour and sugar, were primarily to blame. But changing people's dietary habits, then as now, seemed to be an insurmountable obstacle. No wonder, then, that Dean and others were excited by the discovery of fluoride's impact on teeth.

During the 1930s, Dean, McKay, and colleagues from the PHS and various university dental schools tried to demonstrate fluoride's connection to dental fluorosis and reduced caries rates. Although nobody understood precisely how it worked, and nobody would for a long time, fluoride did indeed seem to change the structure of teeth in a way that offered some protection against the assaults of the 20th-century American diet.

Embarking on a succession of epidemiological studies in towns with fluoride-rich water supplies, Dean gradually zeroed in on a ratio that appeared to offer considerable protection against caries while causing limited and barely discernable fluorosis. The magic number, he determined, was 1 part per million (1ppm)."

Do you find it coincidental that the "right" amount is 1 ppm and not 0.5 or 3.78 ppm?

"Once it became clear that fluoride was the cause of the brown stain, which Dean would soon label dental fluorosis, he shifted the focus of his research, and that of the government's health bureaucracy, from eliminating fluorosis to combatting caries. The rest is history. We are afflicted with taking in or spending lots of time and money avoiding human-added fluoride compounds in our internal environments."

Consider reading the article in full to see the complete evolution of water fluoridation.

They end their treatise on fluoridation with the following statement.

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"In all likelihood, the only significant problem that would arise from an end to fluoridation is that the Florida phosphate industry would have to find a different way - no doubt one more expensive and less convenient - to dispose of its toxic waste."

Why are we not augmenting the water and toothpaste with natural nutrients to support enamel health? Michael Landy, DMD, weighs in on the essential minerals to support healthy teeth.²²⁵ Keep in mind that supporting healthy gums is the most important consideration. Next is the health of the bones that anchor the teeth. Dr. Landy's suggestions benefit both the enamel and supporting bones.

1. Calcium

You may have heard calcium supports dental health without understanding exactly why or how. The body uses calcium to produce a substance known as crystalline calcium phosphate. This mineral compound makes up the hard tooth enamel that surrounds and protects the inner parts of your teeth.

Calcium also plays a key role in bone formation, lending your jawbone the strength and structural integrity to contain the tooth roots in its sockets. Since both enamel and bone wear out with use and over time, the body must keep producing these materials.

Without sufficient calcium in your diet, your tooth enamel may break down faster than it can rebuild itself, making your teeth prone to cavities and other damage. Insufficient bone calcium may also allow the sockets in your jawbone to widen until the teeth become loose.

You can boost calcium intake by consuming more dairy products, including milk, cheese, and yogurt. You may also want to take supplements if you suffer from a condition promoting calcium deficiency. Get plenty of Vitamin D as well, since the body needs this vitamin to use calcium properly.

2. Phosphorus

Phosphorus combines with calcium to form crystalline calcium phosphate. It also supports calcium's role in bone production and remodeling. Without phosphorus, your body can't use calcium well, even with Vitamin D. The results include bone brittleness and teeth that chip easily.

Eating cheese can provide your body with both phosphorus and calcium. You can also get your daily phosphorus by consuming pumpkin seeds, lentils, soybeans, beef, and pork.

3. Magnesium

Magnesium and calcium complement each other to build hard tooth enamel and maintain bone density. Ideally, you should receive a two-to-one ratio of calcium to magnesium daily. If you take supplements of both minerals, measure your daily dosages accordingly.

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Good dietary sources of magnesium include dark green vegetables, legumes, nuts, corn, brown rice, buckwheat, rye, and other whole grains. However, too much magnesium all at once can cause digestive side effects such as diarrhea, so you may need to spread your intake out over the day.

4. Potassium

Potassium is a companion to magnesium in the body's efforts to regulate blood acidity. When your blood becomes too acidic, the acids can remove calcium from your teeth and jawbone, weakening them. A potassium-rich diet can help your teeth and bones use calcium more efficiently.

You can get potassium from many kinds of foods, most notably bananas. In addition, prunes, avocados, potatoes (including sweet potatoes), tomatoes, and Swiss chard can also give you a much-needed potassium boost.

Potassium can also help your teeth in other ways. For example, you may have noticed that some toothpaste contains an active ingredient called potassium nitrate. When this potassium compound enters the tooth enamel, it can reduce pain signals in people who suffer from tooth sensitivity."

Knowledge is freedom. You do not need added fluoride, mercury, CPAP machines, or drilling, and save a dead tooth. Instead, optimizing your health will maximize the health of your blood supply, teeth, gums, and supporting bone structures.

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“Your eyes are the only place in the body where you can see a bare nerve, a bare artery, and a bare vein without doing any cutting. And the disease processes in the eye probably occur in the rest of the body.”

- Andrew Iwach, MD, associate clinical professor of ophthalmology at the University of California San Francisco and executive director of the Glaucoma Center of San Francisco.

Your Eyes are Your Window to Health.

Medicine is divided into tight silos, with very little communication between specialists for a given patient. Steve Jobs is a case in point. At Stanford Medical School, his care was fractured and inadequate. Eye diseases are NOT considered in the context of whole-body health. However, our eyes are a canary for vascular and neurological disorders of all kinds.

A disease may be seen in your eyes at any age, from birth to death, even before you have any symptoms, like vision loss.

Here are three (3) little-known facts about major eye diseases.

- A diagnosis of cataracts is as deadly as a diagnosis of breast cancer.²²⁶
- Macular disease IS a cardiovascular disease.²²⁷
- Glaucoma is Alzheimer’s disease of the eye, and Alzheimer’s is glaucoma of the brain.²²⁸

Although apparently very different, these three eye diseases have a common thread. And that thread in the eye extends to modern society's most common chronic diseases.

Ebola infection provides a poignant clue to the connection. Indeed, Ebola is a deadly pathogen. However, the eye is susceptible to an Ebola infection, and the eye changes that this infection cause provides insights into chronic and acute diseases.

A summary article about Ebola, children, and cataracts by The Seattle Times²²⁹ discusses Ebola-induced eye diseases. Blindness is a dreaded complication of Ebola. In addition, doctors have been shocked to find cataracts in Ebola survivors as young as five.

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“Cataracts usually afflict the old, not the young, but doctors have been shocked to find them in Ebola survivors as young as five. And for reasons that no one understands, some of those children have the toughest, thickest cataracts that eye surgeons have encountered, along with scarring deep inside the eye.

Before the Ebola epidemic in West Africa from 2013 to 2016, doctors did not realize how much damage the disease could leave in its wake because previous outbreaks were small and had few survivors. As a result, eye disease, with the specter of blindness, has become a dreaded complication.

There are about 17,000 Ebola survivors in West Africa, and researchers estimate that 20 percent have had severe inflammation inside the eye, uveitis. It can cause blindness, but cataracts can quickly follow even if it resolves and sight returns. Usually, just one eye is affected.”

Key take-home points from this unfortunate circumstance are,

- The infection causes severe inflammation and uveitis inside the eye.
- The cataract is an amyloid formation in the body's response to this infection and inflammation.
- Amyloids are antimicrobial peptides. The translation of an antimicrobial peptide is a natural antibiotic.
- The cataract, although interfering with vision, is there to save the eye and the person from the infection.
- The eye, being transparent, affords easy observation of amyloid formations (cataracts).
- When amyloid is in the eye may also be throughout the body. So what else explains why people with cataracts die young?

Cataracts reflect a sick eye in a sick body. People with cataracts in the lens of their eye probably have "cataract-like" plaques throughout their bodies.

How does medicine test for amyloids in the body other than through observing eyes? Mayo Clinic indicates a biopsy is required. “A tissue sample is taken and checked for signs of amyloidosis. The biopsy may be taken from the fat under the skin, the abdomen, bone marrow, or an affected organ such as the liver or kidney. Specialized testing of the tissue can help determine the type of amyloid deposits.”

Amyloids are very seldom measured. As a consequence, they are not well understood, but it is quite clear that amyloids are an indication of active infection.

Acute vs. Chronic Disease Detected in the Eye

Ebola stimulates an acute response in the eye - a cataract.

What does this mean for people with age-related cataracts? It is caused mainly by the same process as Ebola - an infection. But, in the case of older people, the infection is chronic and low-grade. People with cataracts are utterly unaware of

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this relationship because modern medicine does not recognize chronic infection as a disease-causing process.

The eye offers tremendous potential for screening populations for brewing chronic diseases. Unfortunately, medicine is slow to adopt new ideas even when they are not new. Global experts understand the value of the eye in diagnosing a disease before it becomes a crisis.

Here is what the experts say about the eye as a window to your health:

“Ever-increasing specialization is made necessary and inevitable by the information explosion of our times. It is, under these circumstances, easy to lose sight of the underlying interconnectedness of things. Yet, this same information explosion has paradoxically enabled us to see more unity within the diversity. We find that medical problems that may seem different or independent when viewed at a superficial level are manifestations of a common underlying pathophysiologic mechanism acting simultaneously at different sites throughout the body.”²³⁰ - Daniel H. Gold in “The Eye in Systemic Disease.”

“There are many systemic diseases we see in the eye,” said Dr. Roy Chuck, chair of the department of ophthalmology and visual sciences at Albert Einstein College of Medicine and Montefiore Medical Center in New York City.²³¹

“The eye is quite literally a “real window” to the rest of the body,” according to Dr. Noel Bairey Merz, director of the Women’s Heart Center at Cedars Sinai Heart Institute in Los Angeles. “The vitreous fluid is clear, and we can look through the opening in the iris and see the blood vessels quite easily,” she said. “They taught us in medical school to look with the ophthalmoscope as part of the general exam. But, sadly, it’s not done by most practitioners, and they have lost the skill set.”²³²

“Diagnosing illness through the eye is nothing new,” according to Dr. Marco Zarbin, chief of ophthalmology at the University of Medicine, Dentistry, New Jersey. “It happens all the time,” he said, “from rare conditions to diseases like multiple sclerosis, leukemia, and brain tumors.” “If you look at your brain, two-thirds of it is dedicated to some aspect of vision,” said Zarbin. “It’s a big deal.”

The retina is a piece of the brain that has grown into the eye and processes neural signals when it detects light say University of Pennsylvania researchers.²³³ Ganglion cells carry information from the retina to the higher brain centers. Other nerve cells within the retina perform the first visual world analysis stages. With the support of different types of cells, the axons of the retinal ganglion cells form the optic nerve and carry these signals to the brain.²³⁴

“The eyes truly are unique real estate,” says Andrew Iwach, MD, associate clinical professor of ophthalmology at the University of California San Francisco and executive director of the Glaucoma Center of San Francisco. “They’re the only place in the body where you can see a bare nerve, a bare artery, and a bare

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vein without doing any cutting. And the disease processes in the eye probably occur in the rest of the body.”²³⁵

With all this information about the connection between the eye and systemic diseases, what advice do doctors provide?

General Practitioner: Their advice is to see an ophthalmologist or optometrist.

Ophthalmologists: These doctors come under the umbrella of surgeons. Not surprisingly, most doctors suggest surgery if they see a cataract. They may recommend eye drops or a laser procedure if they see signs of macular disease or glaucoma. Everything they recommend is eye only. You will not be told about the systemic ramifications of your condition.

Optometrists: These doctors will complete an eye exam and confirm an eye diagnosis. They most likely will prescribe some type of eye drops. However, they will not tell you about the possible systemic connection between eye pathology and systemic risk.

Unfortunately, the patient winds up in a merry-go-round of decaying eye and whole-body health. Cardiovascular disease and cancer are the #1 and #2 killers. The eye is particularly predictive of cardiovascular diseases if only you or your doctor would tell you. Unfortunately, most doctors are not aware of this connection either.

My mentor, the Ophthalmologist from Harvard, Dr. Clement Trempe, showed how the eye could predict certain cancers. His research and clinical work saved thousands of lives. The work of Dr. Trempe and others who screened for cancer risk by observing specific eye freckles is documented in a story by Alfred Thigpen in the Washington Post.²³⁶

"During one of these last summers, retina specialist Neal Adams caught me totally off guard. After examining the back of my eyes for a suspiciously long time, he advised me to schedule a colonoscopy."

"A what?"

"My colon has something to do with my eyes?" I asked.

"The doctor told me he had found "freckles" on my retinas. "When the freckle has a certain appearance and is found in a certain number, evidence shows that it's highly associated with a specific syndrome of colon polyps," he said.

Adams explained that the likelihood of cancer was low but that it was better to be safe than sorry. "It's for your peace of mind," he said reassuringly.

I located a gastroenterologist that afternoon.

This eyeball-colon correlation was news to me and almost everyone else. But, as Adams later told me, it's been known for a long time.

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Richard Cabot, a physician at Massachusetts General Hospital, first reported an association between colon cancer and a particular type of retinal pigmentation in 1935.

“The medical literature remained largely silent on this association until 1980 when Drs. Norman Blair and Clement Trempe described the association between colon polyps and colon cancer and this specific back-of-the-eye freckle,” continued Adams, who is editor in chief of the medical journal *Eye Reports*. They named the freckle CHRPE (pronounced “chirpy,” an abbreviation for “congenital hypertrophy of the retinal pigment epithelium”).

A later study found that CHRPE has a “statistically significant” correlation with hereditary colon polyps known as familial adenomatous polyposis or FAP. It may be that the freckles are caused by the same genetic mutation that produces the polyps.

A 2010 *American Journal of Gastroenterology* study concluded that patients with such freckles should be referred for colonoscopies.

The gastroenterologist I visited did not acknowledge any connection between retinal freckles and colon disease. But he did say that at 63, I was overdue for a colonoscopy, and he worked me into his schedule within a week.

During the procedure, he located and removed three sessile (or flat) polyps, each about the size of a pencil eraser. He sent them off to be tested for malignancy and told me it would take a week to get the results.

Rather than fret about the possibility of a positive from the lab, I focused on discovering more about what still seemed to be a peculiar way to start a diagnosis. I asked Adams more questions.

“When we look in the back of the eye at the retina, we can find signs that may help us identify many disorders — common ones like high blood pressure and diabetes, rare genetic disorders, and even life-threatening cancers.” He said these could include lung, breast, pancreatic, brain, lymphoma, multiple myeloma, and more.

Adams told me he once diagnosed early-stage leukemia in an otherwise healthy person by noting blood spots in the patient’s retina. Another patient’s suspiciously inflamed retinas led him to run an electroretinogram test, which found an abnormality strongly suggestive of a malignancy. He sent the patient to an oncologist, who diagnosed ovarian cancer.”

As Gregory Wolfe, chair of the American Optometric Association’s health promotion committee put it;

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"The eyes aren't just the window to the soul. "The eyes can be the oracles of a variety of systemic conditions," he said.

And more than the eyes are involved. For example, as many of us have read, periodontal or gum disease is associated with heart disease. But few of us are aware, Wolfe and Adams noted, of the associations between periodontal disease and osteoporosis or Alzheimer's disease. Even though people are becoming increasingly cognizant of the interrelatedness of conditions, Wolfe said, the public still sees fields such as dentistry, eye health, and gastroenterology as essentially distinct.

"It's imperative to change the mindset to a more holistic approach," he said.

A recent study by Consumer Reports found that Americans are growing increasingly likely to put off or skip critical diagnostic tests, often for financial reasons. Of course, no one suggests that an eye exam is any substitute for a colonoscopy or that a dental checkup replaces an EKG. But what's disturbing is that Americans may increasingly skip both, with dangerous consequences.

My polyp tests came back from the lab. Two were benign; the third was a tubular adenoma, often called a precancerous polyp. Interestingly, my polyps were not the kind associated with FAP, the syndrome my ophthalmologist had been concerned about. Nevertheless, the advice to get a colonoscopy was worthwhile because colon cancer almost always starts as a benign polyp gone wrong. By removing the polyps, I'd headed off that possibility."

An important statement in the Post article helps us understand why change occurs very slowly in healthcare.

"Of course, no one suggests that an eye exam is any substitute for a colonoscopy or that a dental checkup replaces an EKG."

It is all about conditioning, indoctrination, and believing what is available is best-of-breed. But unfortunately, this cannot be the case because we are collectively so sick.

How can we evaluate a diagnostic test? In the current sick-care system, diagnosing a symptom or disease manifestation is sufficient. These tests answer the question, What? Drugs and procedures are then applied to "solve" the problem. In a revolutionary healthcare system, the diagnostics must shed light on the causes, not the symptoms. These tests answer the question, why?

- Is a colonoscopy superior to an eye exam diagnostically?
 - Colonoscopy illuminates "**What**."
 - Eye exams illuminate "**Why**" (Ebola and chronic infections, for example).

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- Is an EKG superior to an oral checkup?
 - EKG explains, "**What.**"
 - Oral checkup elucidates the "**Why**" (for example, spirochetal infections).

A 2022 editorial by a group of medical doctors and researchers from around the globe provides a much-needed call to action concerning the eye as an early warning system for whole-body diseases. The title is "The Eye Is a Window to Systemic and Neuro-Ophthalmic Diseases."²³⁷ The authors state:

"Ocular involvement is a common and well-known presenting or defining manifestation of **many important systemic** and neuro-ophthalmic diseases, including multiple vascular, rheumatologic, neoplastic, degenerative, inflammatory, and infectious diseases. Thus, ophthalmologists should know the close relationship between various systemic diseases and their ophthalmic and neuro-ophthalmic manifestations."

This introductory statement to the editorial is so vital that it is reiterated as a bulleted list. The diseases inferred by eye diseases are:

- systemic diseases;
- neuro-ophthalmic diseases;
- multiple vascular (what whole body disease is not vascular?);
- rheumatologic (joint / bone diseases);
- neoplastic (cancers);
- degenerative (this includes all brain diseases, including Alzheimer's and other dementias);
- inflammatory diseases (again, what chronic diseases are not inflammatory);
- infectious diseases (This statement is a substantial departure from traditional medical dogma. Implied by infectious disease here is really chronic infectious diseases, as the other diseases on the list are all chronic. Infectious diseases being on the list is finally a move in the right direction. But is anyone listening?).

Interestingly the authors say that the eye involved in systemic diseases is well-known. Has your regular, eye, or functional doctor ever told you this? A researcher refers to the work of other researchers. "Well known" means it is well known in research circles but not in the clinic.

The list of contributors to this publication represents the traditional medical establishment. If only they practiced what they preach.

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- Department of Ophthalmology, University of Texas Medical Branch, Galveston, Texas, US
- University of Texas MD Anderson Cancer Center, Houston, Texas, US;
- Texas A and M College of Medicine, Bryan, Texas, US;
- Department of Ophthalmology, The University of Iowa Hospitals and Clinics, Iowa City, Iowa, US.

This is a key paragraph from the article.

“This special issue of the journal will highlight and review some of the new and interesting ophthalmic and neuro-ophthalmic presentations of vascular disease. Systemic diseases are typically associated with multiple risk factors, including age, smoking, diet, exercise, and chronic inflammation. One of the most common diseases of the eye, age-related macular degeneration (AMD), is associated with many of these same risk factors, one consistent with an underlying “common soil” hypothesis.²³⁸

In addition, new and emerging information has implicated an increased incidence of cardiovascular complications (e.g., myocardial infarction and stroke) in patients with AMD.²³⁹ Hence, managing underlying modifiable risk factors (e.g., smoking, diet) could presumably slow the incidence or progression of both AMD and cardiovascular diseases. Mauschitz et al.²⁴⁰ discuss the many studies supporting this “common soil” hypothesis in this issue.

The “common soil” hypothesis dates back to the 1990s.²⁴¹ Another expression for “common soil” is “internal terrain.” Really, it is just an expression that refers to the extent and efficacy of our immune systems. The major medical associations, through their websites, indicate risk factors. Most of these risk factors overlap across the medical silos established by the associations. The risk factors presented by each group is the common soil. Sadly, the prevalence of these diseases has only worsened over the past couple of generations, indicating that we are ineffective at overcoming the risks of the common soils or the common soils are incompletely defined. And the interventions being offered by your doctor do not impact common soils. A statin drug or blood pressure medicine does not solve your smoking, diet, and exercise issues. Common soil theory suffers from the same limitations as every other intellectual pursuit - garbage in, garbage out.

Your eyes share “common soil” with the most prolific chronic diseases.

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Clayton Christensen, the author of “The Innovators, Dilemma,”²⁴² provides a plausible explanation as to why concepts like the eye used to measure health are not incorporated into the standard of care. He wrote an article in the Harvard Business Review titled “Will Disruptive Innovations Cure Health Care?”²⁴³ His fundamental teaching is that disruptive innovation takes complex ideas and makes them understandable and available to regular folks. Examples he cites are the computer mainframes and push cards evolving to the laptop (or iPad) or George Eastman’s inventions making amateur photography widespread.

In medicine, disruptive innovation brings technology to lower-level healthcare care workers who can obtain sophisticated analyses that are easy to interpret. Nurses, medical assistants, technicians, and physicians’ assistants are examples. The American Medical Association has fought hard on behalf of doctors to prevent less well-trained providers from penetrating their turf. However, technological advancement always leads to change. In healthcare, advancing technology brings elegant yet simple methods to the clinic. For example, new wearable devices bring health information directly to the consumer and bypass medical professionals.

Specialists' visits are now a regular part of the care model compared to decades past. The diagnosis delivered by specialists is more precise but much less accurate as the “common soil” is frequently disregarded. If it were not ignored, the need for specialists would diminish. The “specialist” model is NOT working. Humans are complex but also 99.9% the same genetically. Breaking medicine into protected siloed fiefdoms hampers innovation and allows specialists to sit in an “ivory tower” without adequate accountability for patient outcomes. They only answer to their specialty societies that have their back because everyone is doing the same thing. It is, by definition, insanity.

Sick Eye in a Sick Body

The Eye explains our rate of aging, according to a study sponsored by the National Institutes of Health (NIH) and other organizations worldwide. The NIH funded a formal trial on eye diseases in the 1990s. That trial was called the AREDS, short for the Age-Related Eye Disease Study. The goal of AREDS was to learn about macular degeneration and cataract, two leading causes of vision loss in older adults. In addition, the study looked at how these two diseases progress and what their causes may be.

The AREDS study involved 11 medical centers with more than 4,700 people enrolled across the country. The study was supported by the National Eye Institute, part of the Federal government’s National Institutes of Health. An unexpected result came out of AREDS. Certain eye diseases are predictors of premature or early death (mortality). In other words, this study revealed that a rapidly aging eye occurs in a rapidly aging body.

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Eye diseases are not isolated from the rest of the body.

Eye pathologies serve as biomarkers for whole-body disease.

During a follow-up of 6.5 years, 11 percent in the AREDS study with eye conditions died. This rate of death is similar to that of breast cancer. Has anyone sponsored a cataract or macular degeneration walk for these deadly diseases?

There are no purple ribbons for eye diseases, but they are just as deadly!

Participants who had advanced age-related macular degeneration (AMD) compared with those who had few, if any, drusen (an indicator of AMD) had increased mortality. In addition, more advanced AMD was associated with excessive cardiovascular deaths compared to people without advanced AMD. Is it possible that Mr. Russert (the famous “Meet the Press” host) had AMD, but no doctor knew the connection between this presumed “eye only” disease and heart disease?

In addition to AMD, people with deteriorating vision (loss of visual acuity) died sooner than those with perfect vision. The cause of death was most often cardiovascular.

Authors of one part of the AREDS studies stated: “Nuclear opacity and cataract surgery were associated with increased all-cause mortality and cancer deaths.” The authors concluded that “the decreased survival of AREDS participants with AMD and cataracts suggests these conditions may reflect systemic processes rather than only localized disease.”²⁴⁴ This was a progressive statement back in 2004. Many years later - crickets!

Why isn’t this information reaching the clinic and the public?

Figure 7.1 shows the Age-Related Eye Disease Study data illustrating high mortality associated with eye diseases.

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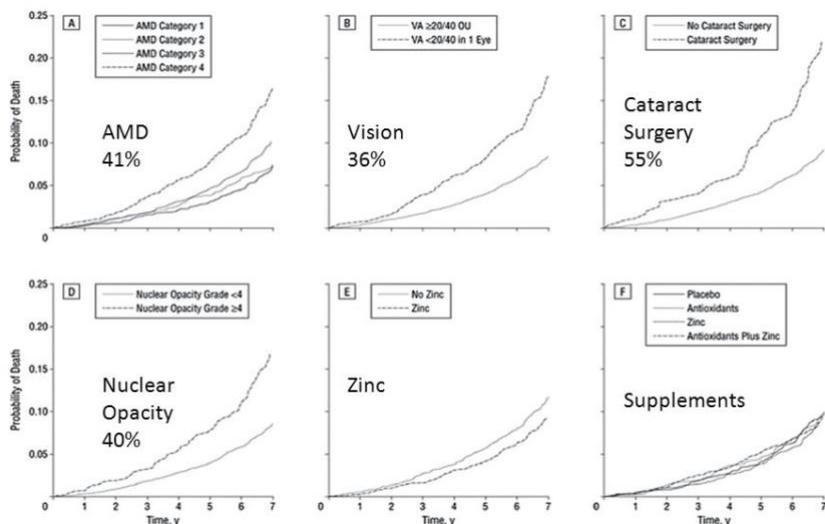


Figure 7.1. Age-Related Eye Disease Study (AREDS) data. The higher the curve above the zero baselines, the higher the death rates associated with the eye condition.

Eye Disease and Early Death

The eye is a predictor of cardiovascular disease. It is also a strong predictor of Alzheimer's disease.³ Dozens of other studies repeat and corroborate the eye/disease/mortality connection discovered in the AREDS study:

The Priverno Eye Study. This was a population-based cohort study of the incidence of blindness, low vision, and survival. Lens opacities are associated with a higher risk of death. The purpose of this study was to investigate further the relationships between different types of lens opacity and patient survival. The analysis of the Priverno data confirms an association between lower survival and cataracts, particularly those confined to the lens nucleus and those that had already prompted surgery. An example research article is "Association between lens opacities and mortality in the Priverno Eye Study."²⁴⁵

The Barbados Eye Study. This study aimed to determine the incidence and risk factors for each leading cause of visual loss in an African-Caribbean population. The incidence of visual impairment was high, significantly affected quality of life, and was a marker of early cardiovascular death. Age-related cataracts and open-angle glaucoma caused $\sim 75\%$ of blindness, indicating the need for early detection and treatment. The connection between metabolic and cardiovascular disease and

3 Lewis, Thomas J., Trempe, Clement L. "The End of Alzheimer's. The Brain and Beyond."

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ocular indications and diseases is strong. An example of a research paper that resulted from the Barbados Eye Study is “Lens opacities and mortality: The Barbados Eye Studies.”²⁴⁶

The Blue Mountain Eye Study. This was the first extensive population-based assessment of a representative older Australian community sample of visual impairment and common eye diseases. The findings demonstrate the connection between the eye and systemic diseases. In particular, cardiovascular risk factors were prominent for eye diseases, including Cataracts, macular degeneration, Glaucoma, and retinopathy. An example of a research paper that resulted from the Blue Mountain Eye Study is “Open-angle glaucoma and cardiovascular mortality: the Blue Mountains Eye Study.”²⁴⁷

The Beijing Eye Study. The Beijing Eye Study is a population-based study that included 4439 subjects initially examined in 2001 through blood tests and visual assessment. The data suggest that glaucoma, particularly angle-closure glaucoma, may be associated with an increased mortality rate in adult Chinese in Greater Beijing. An example of a research paper that resulted from the Beijing Eye Study is “Mortality and ocular diseases: the Beijing Eye Study.”²⁴⁸

The Beaver Dam Eye Study. This study is funded by the National Eye Institute, one of the 20 National Institutes of Health. The purpose of the study is to collect information on the prevalence and incidence of age-related cataracts, macular degeneration, and diabetic retinopathy, all common eye diseases causing loss of vision in an aging population. The study was designed to discover (or detect) the causes of these conditions. The study also has examined other aging problems, such as a decline in overall health and quality of life and kidney and heart disease development. The study revealed that after controlling for age and sex - nuclear sclerotic cataract severity, cataract surgery, and visual impairment are risk indicators for poorer survival (unexpected early mortality from vascular complications).²⁴⁹

The Rotterdam Eye Study. This study started in 1990 in a suburb of Rotterdam among 10,994 men and women aged 55 and over. Major risk factors found for macular degeneration included atherosclerosis (cardiovascular disease). Retinal venular (microvessels) diameters play a role in predicting cardiovascular disorders. Dilated retinal venules at baseline were predictive for stroke, cerebral infarction, dementia, white brain matter lesions, impaired glucose tolerance, diabetes mellitus, and mortality. In addition, inflammation is part of these diseases. An example of a research paper that resulted from the Rotterdam Eye Study is, “Is there a direct association between age-related eye diseases and mortality? The Rotterdam Study.”²⁵⁰ This paper concluded with this statement, “Both ARM and cataract are predictors of shorter survival because they have risk factors that also affect mortality.”

More than 20 studies on eye diseases, early mortality, and chronic disease are completed or ongoing. The connection can no longer be viewed as simply an

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association. Eye diseases ARE whole-body diseases. The AREDS and Beaver Dam Eye Study results were published decades ago. So why doesn't the public know about this information, and why aren't doctors telling patients about the value of eye assessments in illuminating early mortality risk?

Medicine is highly siloed. If a doctor finds something outside their specialty, it goes unreported and untreated.

In addition, medical researchers are reluctant to share all their information. Therefore, not all data is included in publications. I called Drs. Klein, who did much of the work in the Beaver Dam Study. This study was sponsored and paid for by our government - you and me. I asked them for the "raw data." They refused to send me the data unless I was involved in a funded clinical trial. This type of protectionism will NOT help us treat patients.

The Eyes and Brain

The eye is an outcropping and extension of the brain.

The most compelling and important connections between the eye and the brain are ignored. However, definitive proof for the eye/brain connection is as close as Harvard University Press. "The Retina, An Approachable Part of the Brain," by John E. Dowling,²⁵¹ explains how eyes are part of the brain. According to the Harvard University Press overview:²⁵²

"Dowling draws on twenty-five years of new research to produce an interdisciplinary synthesis focused on how retinal function contributes to our understanding of brain mechanisms."

"The retina is a part of the brain pushed out into the eye during development. It retains many characteristics of other brain regions and has yielded significant insights on brain mechanisms."

Dr. Dowling is no rookie trying to make a name for himself. He is the Gordon and Llura Gund Professor of Neurosciences at Harvard University and Professor of Ophthalmology (Neuroscience) at Harvard Medical School. He is a member of the National Academy of Sciences, The American Philosophical Society, and The American Academy of Arts and Sciences. He also has won The Helen Keller Prize for Vision Research, the Paul Kayser International Eye Research Award of the International Society for Eye Research, and the Glenn A. Fry Medal in Physiological Optics.

Eye pathologies, the physiological changes in the eye, often occur in concert with Alzheimer's disease (AD) and other neurodegenerative afflictions. These changes are not just coincidence or "comorbid" occurrences. It turns out that many of these eye changes are due to the same disease processes that occur in Alzheimer's disease. In layman's terms,

eye and brain diseases are the SAME diseases.

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More importantly, since the eye is so easily accessed compared to any other body tissue, it provides the means to diagnose and study Alzheimer's disease long before it shows clinical symptoms. The eye is also helpful in measuring and monitoring someone with AD.

Formations visible in the lens of the eye portend Alzheimer's disease based on a Harvard Medical School study published in 2003.²⁵³ Harvard performed detailed research to determine the connection between the lens of the eye and the brain and the presence of beta-amyloid protein, the hallmark Alzheimer's biomarker in both tissues. Some of the key findings include the following:

- The Alzheimer's protein is found outside the brain and, in particular, is located in the eye.
- The amount of beta-amyloid (Alzheimer's protein) in the brain matched the amount found in the eye's lens.

The eye, being transparent, affords examination of the lens and retina employing direct or indirect methods. Direct methods are as simple as using a microscope to look deep into the eye at the finest visible structures. More sophisticated methods, like optical coherence tomography, provide even greater detail. This technique is 20 times more precise than MRI and about 50 times less costly. That makes OCT 1000 times better than an MRI for Alzheimer's, eye diseases, and other neurodegenerative diseases.

The retinal nerve fiber layer (RNFL), the connection between the retina and the brain's visual cortex, can also be seen with microscopy and very accurately measured using imaging. The thickness of the RNFL, which contains the axons of the retinal ganglion cells, can be objectively measured with non-invasive imaging techniques. The health of these cells tells us about the health of neurons in the brain.

The retina and brain have areas responsible for cognitive functioning that originate from the same embryonic forward part of the brain (the prosencephalon). Retinal involvement in cognitive functioning is supported by the increased prevalence of glaucoma in patients with Alzheimer's. Other supportive evidence comes from postmortem tissue studies demonstrating retinal nerve cell loss in patients with AD and from studies in living patients that have a reduced number of retinal ganglion cells and associated thinner RNFL thickness when they have AD. These studies make a compelling case for the connection between the processes occurring in the retinal nerve fiber layer and the brain of people with neurodegenerative conditions like Alzheimer's disease.²⁵⁴

The retina and areas of the brain share embryonic origins.

What happens in the eye also occurs in the brain.

Microglia, the brain's primary resident immune cells, share this with the retina. A research team at Massachusetts Eye and Ear has shown that microglia, these

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primary immune cells of the central nervous system, serve as “gatekeepers,” or biosensors and facilitators, of neuroinflammation. As a result, the brain and eyes, as opposed to tissue in other organs, tends to perpetuate inflammation once it is triggered

The concept of perpetual inflammation in the brain is not well understood. However, identifying and reducing the inflammatory process is possibly the most critical factor in treating brain and eye diseases.

In general, microglia have different activity stages that can be associated with either harmful or beneficial effects in neurological disease. Their role and function in disease progression are not well defined, even though activation is shared across a broad spectrum of brain-related disorders, from concussion to Alzheimer’s. Researchers across all fields of medicine have recently begun to elucidate the function of microglial cells in various conditions. For example, in Alzheimer’s, Parkinson’s, and other neurodegenerative diseases of the brain, microglia are thought to be harmful. But, as with any form of inflammation, it is only detrimental when running rampant in response to some underlying insult that is seldom correctly identified or treated

In ophthalmology, it is known that microglial cells are activated in response to several diseases. The microglial cell role in disease is thought to be context-dependent, where they can be either beneficial or harmful. This is the prevailing thinking and may be accurate when “context-dependent” is based on the systemic burden of inflammation and causal factors like chronic infections. SARS-CoV-2 has illuminated the two phases of inflammation.

Phase 1. Inflammation is an immune response to an infectious insult.

Phase 2. Inflammation is piqued beyond what the body is equipped to manage.

In this context, inflammation can be both beneficial and harmful. Usually, inflammation exerts a beneficial effect. However, in a virulent infection in those that replicate at an extreme rate, a storm of inflammation may occur that hastens the inevitable - an unfavorable outcome.

Dr. Trempe and I wrote a peer-reviewed paper explaining the interconnectivity between mild brain maladies and more catastrophic brain diseases at a young age.²⁵⁵ This type of continuum of diseases from young to old and from mild to severe is indicative of a common pathway. Microglial activation and the elevation of specific inflammatory cells are a substantial part of that common pathway. The abstract of that paper is reproduced here.

“The path to sporadic Alzheimer’s is a tragic journey beginning before birth and ending in the most dreaded disease of society. Along the disease path is a myriad of clues that portend AD, many of which are complaints of seemingly unrelated conditions from chronic migraines, mood disorders, eye diseases, metabolic syndromes, periodontal diseases, and hormonal

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and autoimmune diseases. Properly treating, not just managing, these diseases before the onset of dementia may significantly reduce dementia incidences.

Current high levels of health complaints reflect a state of generalized poor health and compromised immunity. During the mid-Victorian era, people were long-lived and healthy, suffering from chronic diseases at one-tenth the rate of people today. Our poor health at any age increases susceptibility to chronic diseases and Alzheimer's.

Infection is involved in many cases of Alzheimer's and other neurodegenerative diseases but is also implicated in many chronic conditions. Scientists looking for causation recognize that Alzheimer's is multifactorial and systemic - not "brain only." Therefore, to slow, stop, and reverse the AD epidemic, the identification and reversal of causal factors must occur across the entire life spectrum of humans. This approach simply considers enhancing the immune status of our bodies and brain and controlling inflammation and infection throughout the whole age spectrum.

Infection is causal, but the root cause is multifactorial and immune health-related. Louis Pasteur stated it best when acknowledging the work of Claud Bernard in 19th Century France, "The seed is nothing, the soil is everything."

Your brain and eyes are more challenging to treat compared to other tissues. No one provides an adequate explanation for this scientifically, but the proof is observable in many who have a sudden or one-time brain injury. Consider this example. A hockey player slams into the boards, banging his knee and head with equal force. The knee quickly rehabilitates, and the athlete skates within a week or two. However, in many instances, the player cannot reenter competition by his brain is still "not right." The athlete experiences a 1-time "insult," a medical term for injury. There is no ongoing insult. So why does the knee heal on a predictable schedule, and the brain may not recover for months, or in some instances, forever?

A group from Australia researched this phenomenon of unpredictable brain healing over the past 30 years. They understand the process and potential solutions but cannot explain the "why" of the persistent brain malady. The paper's title is "The meteorology of cytokine storms and the clinical usefulness of this knowledge."²⁵⁶ Toward the end of the report, they delve into the brain in a section titled appropriately,

"Persistent cytokine storms in the ill brain."

The author's state:

"Moderate but persistent cytokine storms are typical of chronic neurodegenerative states, including post-stroke, post-traumatic brain injury, and Alzheimer's disease (AD). In the weather analogy, cytokines

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are what water is to life. Light rainfalls, like low levels of TNF and IL-1 (cytokines), keep physiology ticking. In moderate amounts, rain outcomes improve, as does self-limiting innate immunity (meaning the immune response ends and things quiet down). But in acute excess or unrelenting moderate amounts, both rain and cytokines can kill.

Both the acute and unrelenting patterns are classified as cytokine storms. Acute systemic cytokine excesses, i.e., those outside the central nervous system (CNS), typically arise from the effects of bacterial or viral pathogen-associated molecular patterns (PAMPs) and are, if not acutely fatal, generally transient. In contrast, when excess cytokine is generated within the brain in sufficient quantities, distinct from entering from outside, the usual type of cytokine storm is an unrelenting moderately raised activity that leads to non-resolving inflammation.”

Yes, that was a bit of a mouth full. However, two important points emerge through observations of people with a concussion and low-grade problems like mood and anxiety disorders.

Part 1. Inflammation in the brain, regardless of what triggers it and irrespective of the level, perpetuates longer than inflammation in other areas of the body. Tissue beyond the blood/brain barrier is more susceptible to inflammation. The eye, particularly the retinal tissue, is beyond the blood/brain barrier.²⁵⁷

Part 2. Because of its apparent heightened susceptibility to inflammation, the brain can experience a perpetual disruption caused by moderate chronic or acute insults. However, this is not the case in the tissue outside the blood-brain barrier.

Immune Privilege of the Eyes and Brain

A Harvard Medical School colleague of Dr. Trempe explains persistent inflammation in the eyes and brain. Dr. J. Wayne Streilein of the Schepens Eye Research Institute was the world's expert on inflammation and the eye. In a lengthy article in the *Karger Gazette*, Dr. Streilein stated:

“Not surprisingly, inflammation, if it occurs within the eye, is a profound threat to vision. In an inflamed eye, light transmission through the visual axis can be impeded and diffracted by leukocytes (white blood cells) and plasma proteins (cytokines). As a result, the visual axis can be distorted, causing the focused light image to fall away from the outer photoreceptor segments. Thus, the dilemma! Inflammation is one of the most important pathways by which immune mechanisms protect tissue against pathogens. It is this dilemma – the need for immune protection and the vulnerability to the consequences of inflammation – that lies at the heart of immune privilege in the eye.”

“Through adaptation, evolution has devised a special form of immune protection (immune privilege) that enables the eye to resist the vast

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majority of pathogens by using processes largely devoid of inflammation, thereby avoiding loss of vision. However, we should remember that adaptations of this type represent biological compromises. In the case of ocular immune privilege, the compromise renders the eye vulnerable to those organisms whose pathogenicity and virulence can only be eliminated with overt inflammation.”

This explanation by Dr. Streilein may not be complete in explaining perpetual inflammation. However, he started the conversation to which others are now contributing. Enter the paper titled, “Good news–bad news: The Yin and Yang of immune privilege in the eye.”²⁵⁸ This paper has some valuable gems that are listed here.

- The eye and the brain are prototypical tissues manifesting immune privilege (IP) in which immune responses to foreign antigens are suppressed.
- IP varies not only with the tissue but with the nature of the foreign antigen and changes in the limited conditions under which privilege can operate as a mechanism of immunological tolerance.
- IP functions normally as a homeostatic mechanism preserving normal function in tissues, particularly those with highly specialized functions.
- However, IP is relatively easily bypassed in the face of a sufficiently strong immunological response. The privileged tissues may be at greater risk of collateral damage because their natural defenses are more easily breached than in a fully immunocompetent tissue which rapidly rejects foreign antigens and restores integrity.
- By suppressing inflammation, the eyes and brain can more easily become infected.
- Inflammation is the result of an immune response. Therefore, if the eyes and brain suppress inflammation, they are more susceptible to infection. This may create a vicious cycle that ultimately leads to inflammation - as a survival mechanism.

The researchers conclude that various degrees of tissue damage occurs when inflammation-quelling mechanisms are breached, relevant to eye diseases. For example, severe tissue destruction from retinal viral infections and other retinal inflammation lead to pathologies like macular degeneration. Additionally, ocular immune privilege and tumor-related immune privilege can combine to permit extensive tumor growth and increased risk of metastasis beyond the eye. This is another way eye diseases increase early mortality risk.

Clinically, this means that any treatment of the brain, including the eyes, requires substantial effort to lower inflammation even when the source of the inflammation is discovered and eliminated. This is why treating eye and brain diseases is a long-term prospect.

Longevity: Why the Eye?

The eye is a transparent piece of tissue. Doctors can use a microscope to look into the eye and observe tissue to assess where you lie on the health-disease continuum. The lens is a powerful magnifying glass and enhances the resolution of instruments that study the eye. For example, the OCT instrument performs the same function as an MRI but has a superior resolution; thus, the disease can be detected earlier with the eye instrument.

Many studies indicate Alzheimer's, glaucoma, and macular degeneration are very similar diseases. Which one starts first? The eye provides convenient, powerful, and inexpensive observation tissue. Thus, even if the illnesses begin simultaneously, the eye provides the earliest opportunity to detect disease genesis.

The retina is a transparent, paper-thin layer of nerve tissue at the back of the eyeball on which the eye's lens projects an image of the world. It is connected by the optic nerve, a million-fiber cable connected to regions deep in the brain. A human retina is less than a centimeter square and a half-millimeter thick.

The 1,500 cubic centimeters human brain is about 100,000 times larger than the retina.²⁵⁹

Most systemic (system-wide) chronic diseases show signs and symptoms in the eye.²³⁰ The retina has the highest metabolic rate of any tissue in the human body, with great vascular density.²⁶⁰ Why would that be the case? The retina contains millions of cells that work together to detect light, turn the light photon into electrical signals, and communicate with the brain to produce vision. These tiny photoreceptor cells are called cones and rods. It takes a lot of energy to convert a photon to an electron. When you are tired, an immediate impulse is to close your eyes. Your brain recognizes how much energy your eyes use. When you close your eyes, you feel immediate relief. It is startling how much energy this tiny tissue uses.

Here is a quick chemistry lesson on the retina. It acts similarly to a semiconductor. When the light (photon) hits the tissue, a quantum mechanical interaction leads to an electron being "promoted," which means elevated to a higher energy level. This higher energy state is unstable and the electron "relaxes" to the lowest energy state possible - called the "ground state." This process releases energy as heat, light of a longer wavelength, or electricity (electron flow). In the case of the retina, electrical flow is the most predominant result of the interaction with a photon. First, part of the reason for the very high blood density is to supply nutrients to support all of the reactions that are occurring. Secondly, this process releases heat, and blood flow is a vital cooling mechanism.

Everyone must obtain a routine eye exam regularly. After age 50, these exams must occur at least every five years. It is important to find an optometrist specializing in eye pathology (most focus on refraction and eyeglasses prescription). Your eye doctors should look for the following, at a minimum.

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- Glaucoma;
- Macular degeneration;
- Cataracts (nuclear, subcapsular, and cortical);
- Detailed retinal evaluation, including retinal nerve fiber layer health (volume and thickness);
- Dry eye;
- Any other eye disease.

The instruments that your eye doctor should use include:

- Slit lamp microscope
- Fundus camera
- Optical coherence tomography

You may have to pay cash for one or more of these tests because the insurance payer does not always cover these tests without a diagnosis. However, these eye tests are extraordinarily predictive of your future health and thus offer tremendous monetary value.

Be forewarned that optometrists and ophthalmologists seldom, if ever, interpret eye data in the context of whole-body chronic health and disease. You might have to read the AREDS or other studies if you cannot get a proper interpretation. Try to find a doctor who understands what these tests infer. A way to qualify an optometrist is to determine if they have an OCT instrument and will accept a cash payment to run the scans. You will need to see an integrative doctor to treat you systemically for "so-called" eye diseases.

Here is a review of the significant biomarkers in the eyes that indicate or predict chronic disease. The characteristics of these eye biomarkers vary from person to person, but standardized classifications for disease progression are available in the literature. The key word here is “classifications” in the plural. There are no absolute standards, and eye doctors can add their personal experience to a diagnosis.

Dry Eye

A dry eye is a condition of altered tear composition that results from a diseased or dysfunctional lacrimal functional unit. Evidence suggests that inflammation causes structural alterations and functional paralysis of the tear-secreting glands. Changes in tear composition resulting from lacrimal dysfunction increased evaporation, and poor clearance has pro-inflammatory effects on the ocular surface. This inflammation is partly responsible for irritation symptoms, ocular surface tissue disease, and altered corneal tissue barrier function in dry eyes.

Today dry eye is treated as an “eye-only” disease like all the other eye diseases mentioned in this section. Inflammation may have a pain-initiating impact on specific tissue, but it is seldom isolated to a single organ. Inflammation is often

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found in the blood of people with dry eyes. All health is connected. A dry eye may be the earliest sign of systemic inflammation.

One cause of dry eye is Demodex mite lid infestation. These particular mites are a culprit in many cases of eye inflammation and can be concurrent with dry eye disease due to their chronic nature. Patients with an ocular Demodex infestation often complain of itching, burning, redness, crusting at the base of the lashes, blurry vision, and dry eye. However, Demodex is not eye-only.

Demodex is considered a tick-like organism. They live in the hair follicles and skin, especially around the face, eyelids, and lashes, and feed on dead skin cells and oils. They can become problematic when they overgrow, creating inflammation. This can cause symptoms like itching and sores and trigger or aggravate skin conditions like eczema or rosacea. Certain types of Demodex live on skin that is thin and wrinkled. That includes the elbows, knees, shoulder blades, around the penis, and under the breasts. Could this class of mites be the reason behind aging wrinkles? Researchers believe there is a wide variety of Demodex mites. They may vary depending on geographic location.²⁶¹

Cataracts

Cataract removal is the most common surgery on the planet. This surgery is performed on nuclear cataracts, but there are other types. Nuclear cataracts interfere with vision more so than other cataracts; thus, they are the most frequently removed. Tables 7.1 and 7.2 and Figure 7.2 provide statistics on the incidence of cataracts and cataract surgery. Interestingly, the “success rate” for cataract surgery is listed at 98%. However, if the doctor advising and performing the surgery did not tell the patient that they are at increased risk for cardiovascular disease and dying young, do you consider the surgery a success?

Not warning a patient about a DEADLY health condition is a failure.

Cataract Statistics	
Number of Americans age 40 and older who are affected by Cataracts	20.5 million
Percent of Americans age 80 and older who have Cataracts	50 %
Annual amount spent by the federal government to treat cataracts through Medicare	\$3.4 billion
Cataract Surgery Statistics	
Average cost of cataract surgery per eye	\$3,279
Number of Americans who have cataract surgery each year	3,000,000
Success rate of cataract surgery	98 %
Percent of patients had no severe postoperative complications	99.5 %

Table 7.1. Cataract surgery statistics.

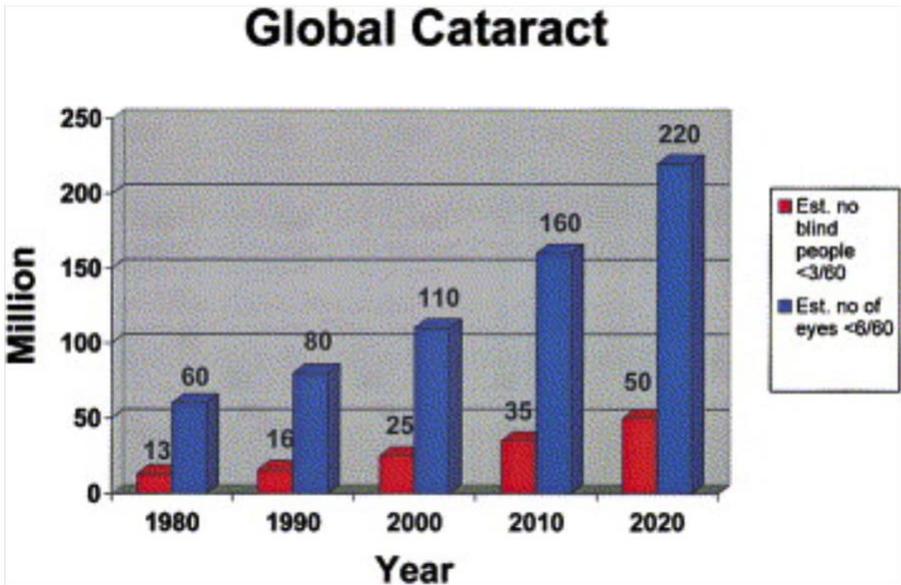


Figure 7.2. Statistics on cataracts as a cause of blindness or visual impairment by year.

Projections for cataract (2010-2030-2050)

Year	All	White	Black	Hispanic	Other
2010	24,409,978	19,514,896	1,973,883	1,761,306	1,159,893
2030	38,737,561	27,866,836	3,428,470	4,745,378	2,696,878
2050	50,231,932	30,781,670	4,966,939	9,510,635	4,972,687
Total Population	142,648,393	103,846,437	15,190,777	14,901,369	8,709,810

Table 7.2. Projections for cataracts in the United States.²⁶²

“The Lens Opacity Classification System III”²⁶³ publication provides cataract classification. Figure 7.3 below gives a grading scale for cataracts. The more severe the cataract, the higher the potential risk of dying young from vascular disease. That information is NOT provided with the grading system.

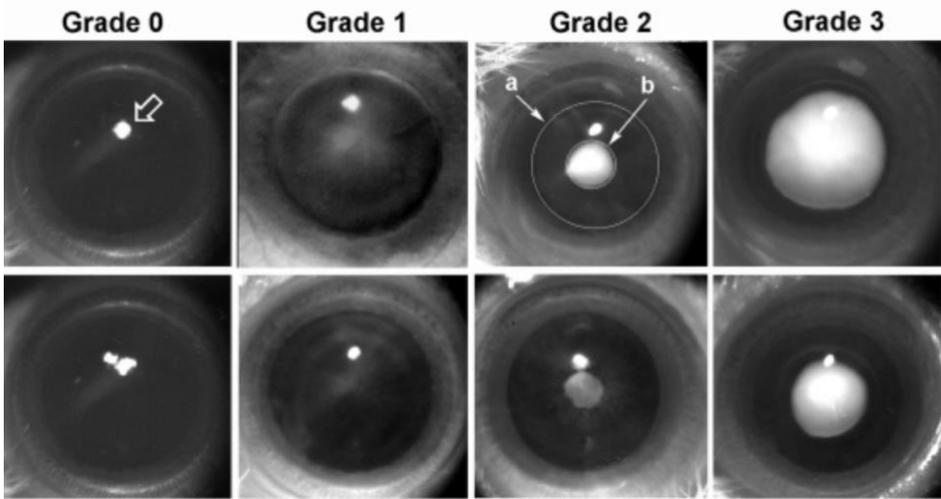


Figure 7.3. Classification of nuclear cataracts from grades 1 – 4.

Cortical cataracts are associated with Alzheimer’s disease. A Harvard Medical School team contributed unequivocal data on this connection.²⁶⁴ Cortical cataracts, also called supranuclear cataracts, are “opacities” in what should otherwise be a clear lens. They occur at the periphery (edge) of the lens, while the more common nuclear cataracts appear in the center of the lens. Figure 7.4 shows Alzheimer’s cataracts from the Harvard research. The white line is a “slit” beam of light that illuminates cataracts, similar to a ray of sunlight that exposes dust in an otherwise dark room.

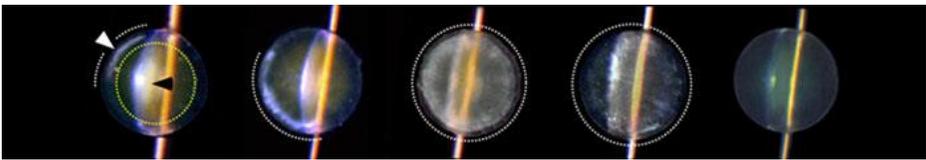


Figure 7.4. “Alzheimer’s” cortical cataracts in the lens of the eye. The white arrow shows the cortical cataract formations, and the black arrow points to the nuclear cataract formation.

The COVID-19 pandemic has profoundly impacted every aspect of healthcare delivery in the United States.²⁶⁵ For example, during the first two months of the pandemic, there was a dramatic decrease in preventative and elective care, which impacted modalities ranging from imaging and procedures to laboratory tests. In addition, the field of ophthalmology was not immune to the impact of the pandemic. Notably, one study using surgical claims processed through Change Healthcare found that cataract surgeries were initially reduced early in the 2020 pandemic year but then rebounded to 2019 volume by the end of the year.

Macular Degeneration

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Macular degeneration (ARMD or AMD) is a slowly progressing disease for age-related macular degeneration. The earliest stage of the disease is called “dry” AMD and is not treated, instead only observed in the standard-of-care. This is true even though dry AMD indicates an increased risk of death, according to the AREDS and many other studies. Also, dry AMD often progresses to the “wet” form. Even worse, wet AMD portends Alzheimer’s disease statistically significantly. Here is a reference to a classification and grading system for macular degeneration and a figure of the stages of AMD.²⁶⁶

Dry macular degeneration is a biomarker for cardiovascular disease.

However, in the standard-of-care, this disease is only observed – not treated - and the patient is not informed of the risk.

Approximately 10% of 50-year-old males have drusen in the retina of their eye. Drusen is a marker for dry AMD. Interestingly, heart disease “mysteriously” takes the lives of many 50-year-old males. The AREDS study suggests that these two are related. Eye doctors can see drusen using inexpensive and non-invasive methods. Doesn’t it make sense to get this and other eye evaluations sooner rather than later? Of course, if you are found “positive” for an eye pathology, you will also need a blood test and a good doctor who can identify the condition’s root causes. Your conventional doctor, who treats symptoms, will not have the slightest clue about the meaning of the eye and blood tests even though the information is well-published by our National Institutes of Health and other prominent sources.

Figure 7.5 shows the progression of macular degeneration from a healthy eye on the left to a “wet” (bleeding) diseased eye on the right. The light-yellow dots are drusen formations. Drusen contain the beta-amyloid protein affiliated with Alzheimer’s disease.



Figure 7.5. Progression of macular degeneration. The small yellow dots are called drusen and are composed of beta-amyloid protein found in the brains of people with Alzheimer’s.

The prevailing treatment for macular disease worsens the vascular problem. As macular degeneration progresses, the existing vessels become diseased. As a result, your body produces new or collateral vessels to ensure adequate blood flow to eye tissue. The standard of care treatment stops the growth of the new vessels. Unfortunately, increased death rates result from this treatment. The treatment mechanism is “anti-VEGF,” where VEGF is an abbreviation for vascular endothelial growth factors. The translation of anti-VEGF is the stopping of new

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or replacement blood vessels. The anti-VEGF treatments are Lucentis, Avastin, and another monoclonal antibody, “mab” eye injectables.

There are so many things wrong with Lucentis, Avastin, and the mabs that it is hard to find a place to start. First and foremost, it does not just “treat” eye diseases. The prevailing approach for the administration of Lucentis is through eye injections. However, the eye is full of blood vessels, and the drug enters the bloodstream quickly, distributing throughout the body. As a result, this drug has severe consequences from a whole-body perspective, even though it is administered through the eye.

Dr. Trempe responded to a New England Journal of Medicine article promoting using Lucentis for macular degeneration.²⁶⁷ The technical name for Lucentis is Ranibizumab. This drug slows or stops the growth of new vessels in the back of the eye, leading to slight improvements in vision – but only for a while and only slightly at best.

The risks associated with Lucentis far outweigh the benefits.

The downside is it stops the growth of new vessels in the rest of the body, some of which save lives when an existing vessel closes or becomes occluded from disease. As a result, Lucentis patients spend more time yo-yoing into emergency rooms, and some die sooner than those not treated. Here is Dr. Trempe’s response:

“To the Editor: In their Clinical Therapeutics article on the use of ranibizumab for neovascular age-related macular degeneration (AMD), Folk and Stone (Oct. 21 issue)²⁶⁸ do not mention the significant risk of death from cardiovascular disease among such patients. However, in the Age-Related Eye Disease Study (ClinicalTrials.gov number, NCT00000145), during a median follow-up of 6.5 years, 534 of 4753 participants (11.2%) died.²⁶⁹ Furthermore, the development of disease in the other eye is common.

In the Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab in the Treatment of Neovascular Age-Related Macular Degeneration (NCT00056836) and Anti-VEGF Antibody for the Treatment of Predominantly Classic Choroidal Neovascularization in Age-Related Macular Degeneration (NCT00061594) trials, in the entire treatment group, the same destructive wet type of AMD developed in the other eye on average within one year in 22% of the patients, within two years in 33% of the patients, and in 5 years in 85% of the patients.²⁷⁰

The risk factors associated with AMD and cardiovascular disease are the same.^{271,272} Treatment to control those risk factors should start early, when drusen are first detected. The goals of treatment should be the following:

- first, to decrease the rate of death from cardiovascular disease;
- second, to prevent the disease from affecting the good eye; and,

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- finally, to treat the eye involved with advanced disease.

Giving repeated intraocular injections to control the disease when it is far advanced is only part of the treatment and causes more harm than good.”

The real question is, should intraocular injections be any part of the treatment? The answer to this question is an absolute NO. The impression is that anti-VEGF treatment dramatically improves vision. This is false. Vision improves marginally, if at all when measured after five years of treatment. And risks of anti-VEGF treatments are seldom discussed with the patient.

Thus, the standard of care feeds a double lie:

1. increased mortality without informed consent about this possibility, and
2. little improvement in vision, despite what patients are led to believe.

Lucentis and Avastin treatments are injuring and killing patients. Damage caused by these drugs is explained in an article titled “Treatment of Exudative AMD: Data from the CATT and IVAN Trials.”²⁷³ Serious adverse events are “mostly hospitalizations.” The text of the article indicates that the types of “events” landing you in the hospital are heart attack and stroke. Is the eye isolated from the rest of the body? Maybe those blood vessels that the artificial anti-VEGF treatment destroys or blocks are there to help and protect you.

Figure 7.6 is from the LUCENTIS® [ranibizumab injection] packing insert. Section 5.4 provides fatal event statistics. Note the statistics on harm are presented as “absolute” values. However, benefits are always presented as “relative” values. The critical early mortality data provided on Lucentis by the manufacturer, Roche Pharmaceuticals, for mortality within the first two (2) years of treatment is,

- 1.2% in the control group,
- 2.8% in those treated with 0.3 mg Lucentis, and
- 4.4% in those treated with 0.5 mg Lucentis.

Using absolute statistics, the increase in mortality from no Lucentis to 0.5 mg is 3.2%. However, using the statistics that the drug companies broadcast to fool an unwary public is,

370% increase in death rate in just two (2) years!

5.4 Fatal Events in DME Patients

A pooled analysis of Studies DME-1 and DME-2 [see *Clinical Studies (14.3)*] showed that fatalities in the first 2 years occurred in 4.4% (11 of 250) of patients treated with 0.5 mg LUCENTIS, in 2.8% (7 of 250) of patients treated with 0.3 mg LUCENTIS, and in 1.2% (3 of 250) of control patients. Over 3 years, fatalities occurred in 6.4% (16 of 249) of patients treated with 0.5 mg LUCENTIS and in 4.4% (11 of 250) of patients treated with 0.3 mg LUCENTIS. Although the rate of fatal events was low and included causes of death typical of patients with advanced diabetic complications, a potential relationship between these events and intravitreal use of VEGF inhibitors cannot be excluded.

Figure 7.6. Lucentis packaging insert, section 5.4 Fatal Events in DME (diabetic macula edema) patients.

Roche describes the primary efficacy endpoint as "the proportion of patients who maintained vision, defined as losing fewer than 15 letters of visual acuity at 12 months compared with baseline."

Note that a patient can lose vision, but it is defined as "maintained vision."

Lucentis and any anti-VEGF drug cause an increased rate of dying young. These drugs also substantially increase "adverse events" associated with continued and prolonged use. Figure 7.7 shows the increase in adverse events from data provided by the manufacturer of Lucentis. These drugs block an important repair and life-saving mechanism, building new vessels around areas where old vessels fail.

Proportion of patients with adverse events

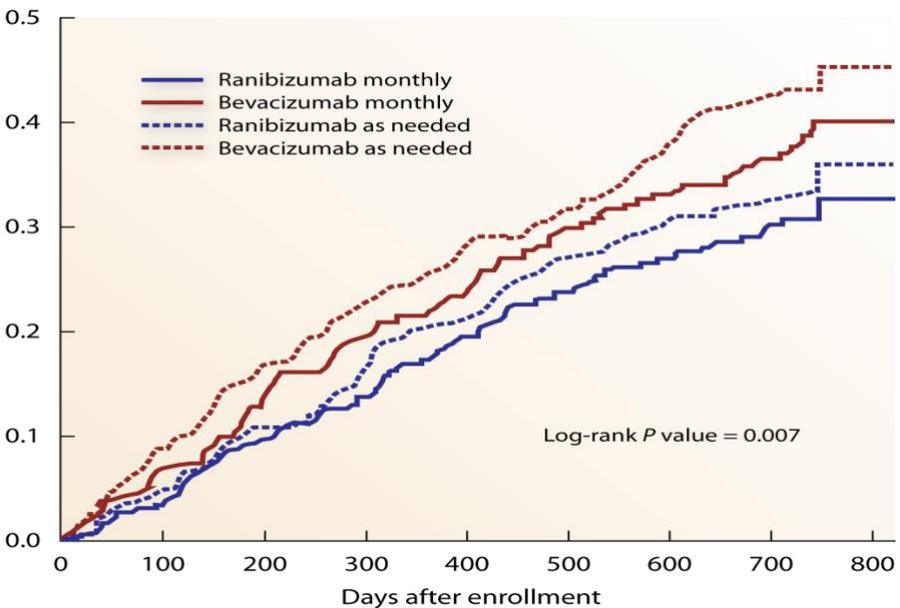
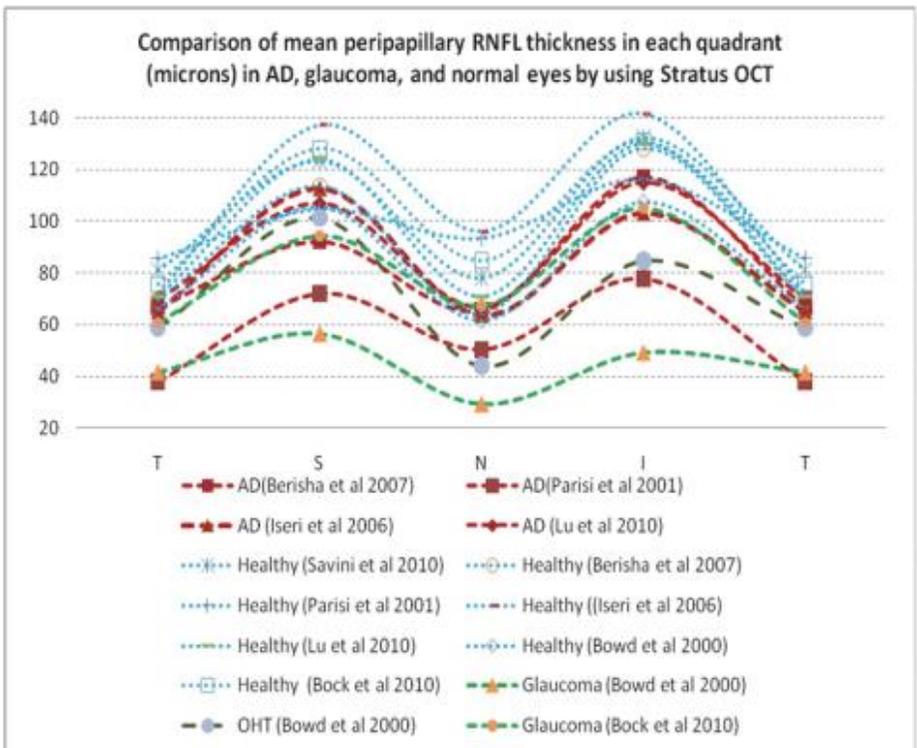


Figure 7.7. Adverse hospitalization events after treatment with Avastin or Lucentis.

Macular degeneration, the main target of Lucentis, is cardiovascular disease. The vessels in the retina (back of the eye) have sufficiently deteriorated that blood oozes from them. Do you think this is happening just in the eye? It indeed is not. The eyes provide an elegant real-time window to watch cardiovascular disease. Cardiovascular disease is an inflammatory disease exacerbated by opportunistic pathogens. Our prescription is to stop Lucentis and measure and treat inflammation and its causes. As a result, your eyes will most likely get better, and you will live a long and healthy life compared to those on Lucentis. My mentor, Dr. Trempe, did this over decades. His patients enjoyed eye and whole-body improvements that were second to none.

Retinal Nerve Fiber Layer

There is a precise diagnostic connection between the loss in thickness of the retinal nerve fiber layer (RNFL) and neurodegenerative diseases like glaucoma and Alzheimer’s disease. Dr. Gordon Plant reviewed this connection in an article titled “Retinal Nerve Fiber Layer Thinning in Alzheimer’s Disease.”²⁷⁴ In addition, over 1000 peer-reviewed medical articles relate Alzheimer’s and the retinal nerve fiber layer. Figure 7.8 shows the difference in the retinal nerve thickness in healthy and diseased cases.



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Figure 7.8. Retinal nerve fiber layer thinning with degenerative diseases. Note that the thickness of this nervous system tissue declines with the two neurodegenerative diseases, glaucoma and Alzheimer's disease. 274

We will unlikely know when the disease “officially” starts. However, it is known that people who died young accidentally (in their 20s) showed the earliest markers for diseases like Alzheimer's when autopsied. In addition, plaques are observed in some of the brains of these young people. Thus, our true goal is to determine when we can first observe disease. Then, hopefully, detection can be pushed to the closest point to disease genesis. This is when any condition is most treatable and reversible.

The advantage of the eye is it can be investigated in great detail, inexpensively, and non-invasively. This is the utopia of chronic disease diagnostics and, more importantly – early detection and diagnosis. People with AMD or RNFL thinning will likely progress to Alzheimer's but often do not have any cognitive loss symptoms when they receive an initial eye diagnosis for nervous tissue loss. These people CAN be helped BEFORE they have symptoms of the disease. This would classically be referred to as “prevention.” But it is not really prevention. It is treatment. Just because a person is not symptomatic does not mean the disease is not present. We must recognize that we all lie on a health-disease continuum. Again, treating as early as possible is your best hope - especially for brain and eye diseases.

Our Eyes Reside in a Connected Body

Humans have but one circulatory system, one nervous system, and one lymphatic system. These systems service our eyes along with EVERY OTHER TISSUE IN OUR BODY. So when our eyes get sick, do you think we are perfectly healthy everywhere else? The answer is NO. We are suffering in our whole bodies too! But you may not be aware of your systemic (whole-body) illness until you suddenly get sick or die.

In 2006, European researchers published a review article titled “A Sick Eye in a Sick Body? Systemic Findings in Patients with Primary Open-angle Glaucoma.”²⁷⁵ Before this publication, few in the medical community recognized glaucoma, a significant neurological disease, as a systemic disease. The assumption was that the disease was isolated to the eye. Now there is recognition that glaucoma is actually a precursor to Alzheimer's disease. It is the same type of disease, but it shows up in the nervous system in the eye before symptoms of brain degradation appear. This time lag may be due to the brain's extraordinary “reserve” compared to the eye's small nervous system. Another explanation is that eye disease measurements are superior to brain measuring instruments.

Despite our recognition of the association between glaucoma and a sick body, no procedures or processes have been implemented to benefit patients. If anything, eye-only philosophies and treatments are expanding due to the 10-minute office

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visit and the marketing behind the drug Lucentis. The abstract of “A Sick Eye in a Sick Body” is replicated here:

“Despite intense research, the pathogenesis of primary open-angle glaucoma (POAG) is still not completely understood. There is ample evidence for the pathophysiological role of elevated intraocular pressure; however, several systemic factors may influence the onset and progression of the disease.

Systemic peculiarities in POAG include alterations of the cardiovascular system, autonomic nervous system, immune system, and endocrinological, psychological, and sleep disturbances. In addition, an association between POAG and other neurodegenerative diseases, such as Alzheimer's and Parkinson's disease, has also been described.

Furthermore, the diagnosis of glaucoma can affect the patient's quality of life. By highlighting the systemic alterations in POAG, this review attempts to bring glaucoma into a broader medical context.”

The authors say that their findings suggest that glaucoma is not just a process involving the visual system but is more likely the manifestation of a more generalized systemic dysfunction. “Glaucoma is a multifactorial disease, and a complex cascade of events and interactions between interocular pressure, vascular, immunological, and various other systemic factors that must be postulated to explain the development of glaucomatous damage.” Interestingly, AD is also viewed as a multifactorial disease. You now should realize that many or most of these “factors” overlap.

In the book “The End of Alzheimer's,” we explain that Alzheimer's is not a “brain-only” disease. Alzheimer's is a sick brain in a sick body. Further, we show how the medical research community understands Alzheimer's is a vascular (heart-related) disease. Thus, our sick eye and sick brain in a sick body are actually a sick circulatory system. And circulatory (heart) diseases continue to be the number one killer.²⁷⁶ When you add brain and eye diseases to the cardiovascular disease category, it becomes the dominant mechanism of human diseases.

A sick eye and brain are symptoms of a sick circulatory system.

All the predominant eye conditions are actually tissue biomarkers for systemic disease. The eye provides the most important health information. Why? Because pathology changes indicate a severe chronic illness is imminent compared to risks or blood biomarkers, Figure 7.9.

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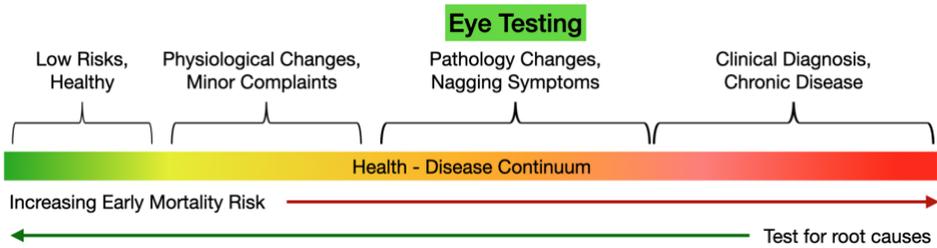


Figure 7.9. The risk biomarker continuum. Pathology measurements obtained by analyzing the eye are closest to a disease diagnosis. Risks and blood-based biomarkers provide more information on root causes.

Eye conditions are a clue that you should delve broader and deeper into your body for why you have an illness. Eye diseases, like all other diseases, do not spring up out of nowhere. Thus, if you have an eye disease, work backward by testing your blood and evaluating risks to determine WHY the eye disease is occurring. Treating an eye condition in isolation is a serious missed opportunity that may catch up to you later in life as other diseases of aging and inflammation “suddenly” develop

Eye tests explain where you lie on the health-disease continuum.

Chapter 8: Energy Medicine

"In every culture and every medical tradition before ours, healing was accomplished by moving energy."

- Albert Szent-Gyorgyi

Energy Medicine

If you want to understand health, energy is fundamental. Our bodies are biological, for sure, but biology is there to drive electricity. Electricity is energy. The only real and useful ongoing source of energy on our small planet is derived from the Sun. Harness the Sun's energy is fundamental to health. Do you view energy is that obtained from food only? We need food for energy, but we have adapted to absorb energy directly from the Sun as well. Most people in the west are unaware of the value of energy medicine, what it does, and how it works in harmony with our biology.

What is the best way to obtain an energy medicine treatment? You want some proven method that is safe, effective, and inexpensive, right? You also want to work with a practitioner who is competent and experienced. The solution that meets all these criteria is to go outside and get PLENTY of sunshine. Your practitioner is God.

I laugh (or cry) at the concept of "renewable energy." Why? Because all energy on earth is renewable as it comes from the same source, but just over a variable time window. That fundamental energy source is fusion. Fusion is the process that powers the sun and the stars. It is the reaction in which two atoms of hydrogen combine, or fuse, to form an atom of helium. The energy produced by nuclear fusion is light waves and heat. The light waves are called photons.

Thus, the one main energy source fueling us and our planet is derived from the fusion reaction.⁴ The equation for that energy is:

$$E = MC^2$$

⁴ Gravity, radioactive decay, and the rotation of the Earth contribute about 0.03% of the total energy on Earth. The Sun contributes the rest.
(https://energyeducation.ca/encyclopedia/Earth%27s_energy_flow)

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Where M is the atom's mass and C is the speed of light. There is a tremendous amount of energy contained in every atom, as expressed by this equation.

The earth is separated from the sun by 93,000,000 miles of vacuum.⁵ A vacuum is a perfect insulator, so the heat generated by fusion on the sun does not cross this vast vacuum to the earth. However, photons have no mass and DO cross the great divide. We know this because we see the visible light photons and feel the infrared photons as heat.

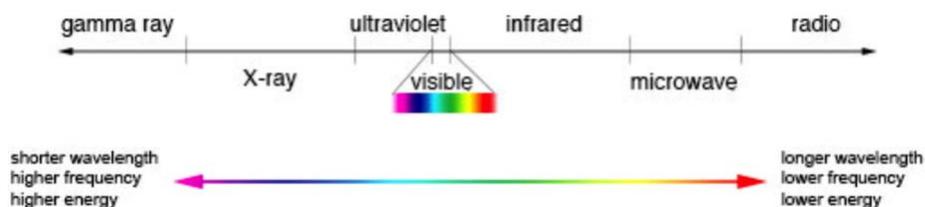
Earth does not make very much energy but gets the sun's energy through the light that hits our small planet. The equation that defines the energy of light is:

$$E = h\nu$$

Here, h is a constant called Planck's constant and ν is the frequency of the specific light.

The only way our planet gains energy is by converting light into a workable form of energy, mainly by plant photosynthesis. But plants are not the only organisms that absorb energy from the sun. So do you. It happens on your skin, eyes, ears, and myriad other photoreceptors and chromophores. The terms photoreceptors and chromophores are a bit limiting as essentially all substances interact with light of varied or specific wavelengths. For simplicity, the terms photoreceptor and chromophore are appropriate for those substances most associated with the absorption of the sun's energy. Thus, both plants and animals have receptors that can interact with and absorb energy from light.

Light is NOT just in the form we see, that is, visible light. Do you see the oxygen you breathe that drives your metabolism? Of course not. Much of the energy from the sun comes in light energy packets that we DO NOT see. Infrared light carries more than half the energy that reaches earth. We cannot see infrared light, but we can feel it as heat. Figure 8.1 show the wide range of light waves (photons) that come from the sun and hit the earth.



⁵ Heat or "temperature" is the measure of the average of the movement of substances (particles) referred to as their kinetic energy. In order for heat to be transferred and move from one place to another, there must be particles present. In a vacuum, for example between the earth and the sun, there is no way to deliver heat through normal classical means. That is, by the exchange of energy between particles because there are no particles in a vacuum.

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Figure 8.1. Range of photons (light waves) that come from the sun. The light contains a range of photons with various frequencies. It is the frequency of the light that determines the energy it contains. For example, a single gamma ray has 10,000,000,000,000,000 (10 quadrillions) times more energy compared to a single radio wave.

NASA explains the electromagnetic (EM) spectrum tangibly. "The electromagnetic (EM) spectrum is the range of all types of EM radiation. Radiation is energy that travels and spreads out as it goes – the visible light that comes from a lamp in your house and the radio waves that come from a radio station are two types of electromagnetic radiation. The other types of EM radiation that make up the electromagnetic spectrum are microwaves, infrared light, ultraviolet light, X-rays, and gamma-rays."²⁷⁷

"You know more about the electromagnetic spectrum than you may think. Figure 8.2 shows where you might encounter each portion of the EM spectrum in your day-to-day life."

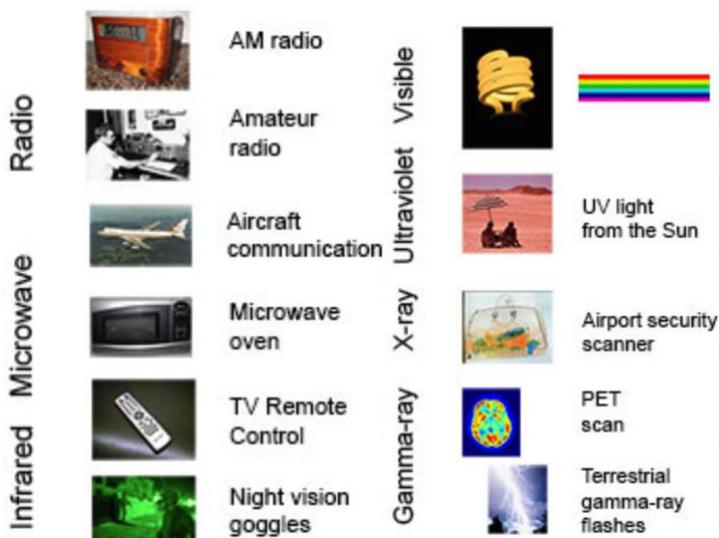


Figure 8.2. Electromagnetic energy types and how they may be observed with various devices.

The basic equation for energy explains that as the frequency increases, so does the wave's energy. All light, regardless of the energy it carries, travels at the same rate of speed, 300,000 meters per second. The shorter the wavelength, the higher the frequency. Hence, frequency and wavelength are inversely proportional to each other. The wavelength determines the number of wave crests passing a given spot in one second.

Importantly, like the tree falling in the woods, which no one hears, light that does not land on something that can interact with it retains its energy. However, light

can interact with substances it hits if there is a frequency match between the substance and the light. The energy the light possesses and the intensity of the light produced by its source have a profound potential impact on whatever it touches and with which it interacts. The two, frequency and intensity, go together.

NASA explains the different energy frequencies in ways we humans can observe the effects, assuming there is an interaction. For example, a radio wave of a specific frequency interacts with a Bluetooth device to send data to a receiver in a radio to produce sound waves that we hear. Bluetooth uses short-wavelength UHF radio waves of a frequency range between 2.4 and 2.485 GHz. There is no data transfer if there are no waves or interactions with a receiver. Thus, there is a yin and yang. Waves of light are everywhere, but there has to be a receiver that can interact with the specific wavelength(s) being sent. Otherwise, the signal will either bounce off or pass through, and nothing will happen. That is, there is no interaction.

Light as "Electro" Energy

When it comes to light, thus energy, there are two considerations.

1. Lightwave frequency: The frequency of the light is depicted in Figure 8.1. Light of short wavelengths is higher in energy than that of long wavelengths.
2. The intensity or concentration of the light. Thus, a tiny amount or concentration of high-energy gamma rays may be of little concern to our health, whereas high concentrations of low-energy microwaves may be of great concern.

Each of us experiences the light energy from the sun daily.

- We see things because our eyes have photoreceptors for visible light waves.
- We hear things because our ears have photoreceptors for sound waves.
- We feel warmth because our skin has photoreceptors for infrared light waves.
- Our skin darkens because it has photoreceptors for ultraviolet light waves.

Light IS energy, and we have evolved and adapted to interact with ALL wavelengths of light produced by the sun. Also, we have adapted to the intensity of the light for each wavelength that reaches the Earth's surface. Anything different than this, except within modest variations, is unnatural. Thus, one way to look at this is that any light energy that is not equivalent to that of the sun in terms of intensity and frequency could be as unnatural as taking a pharmaceutical drug. Some drugs provide more good than harm, while others provide more harm than good.

Certain interactions between light and you are not noticeable. For example, your skin, your largest organ, interacts with light to convert the cholesterol molecule

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to vitamin D. Serotonin is also manufactured within your skin by the action of light on your physiology. Melatonin is produced when light does not reach your eyes. It is also manufactured in your mitochondria through the action of infrared light on cytochrome c oxidase. "Cyto" means cell, and "chrome" means light; thus, cytochrome means a light-absorbing cellular substance. This process will be discussed in detail later in this chapter.

Light is a catalyst for reactions in your body, most notably, your skin. In some respect, light performs a similar function to enzymes. Light, like enzymes, make physiological reactions in your body happen more easily or happen when they otherwise would not occur.

Another definition of energy is work. Consider this simple experiment. Carry a big bucket of water up a hill. You must expend energy to get the water uphill. Now pour the water onto the top of a water wheel connected to an electric generator and a light bulb. You, through your work, can convert your energy, which originated from food, which originated from sunlight - back into light energy as the bulb illuminates when the turbine rotates. This is an inefficient process, with some energy being lost with each step you take. Greater efficiency is realized when our bodies turn light directly into energy. It is always best to avoid the middleman.

How Our Body Converts Energy to Work

Three important concepts explain the use and conservation of light-derived energy. These factors drive our body's internal energy, repair, and recovery reactions. They are:

Exothermic reactions. This type of reaction is like burning wood. Once the fire starts, energy is released, and we see that as light and feel it as heat. The heat we feel comes from two sources: 1. The infrared light released by the fire that hits and interacts with our skin to release energy as heat; 2. The heat from the fire warms the surrounding air, and that warmer air heats our skin through conduction.

Endothermic reactions. This type of reaction requires constant energy input for the reaction to occur. For example, in the case of the water wheel, you had to expend energy to get the water to the top of the wheel. This created "potential energy" that, upon being poured onto the top of the device, released that potential and converted into usable work energy. However, when the bucket is empty, the light goes out. Therefore, water must be continuously poured on the water wheel to keep the light bulb burning.

Activation barrier. Essentially all energy-producing reactions require a "push." That is, they do not just spontaneously occur. Consider mixing gasoline and oxygen in your car's engine, for example. The reaction between these two chemicals releases a significant amount of energy, which is an exothermic reaction. However, the reaction does not start without a bit of help. A spark from a spark plug is required for the reaction to move forward. In this way, a spark plug

is a catalyst for the reaction. Enzymes within your body perform the same function as the spark plug. They are catalysts to initiate critical reactions. Likewise, light can act as a catalyst for a reaction and, in this respect, is like an enzyme. In some instances, the light activates enzyme molecules that give biological reactions the needed push to move forward.

In your body, exothermic and endothermic reactions occur all the time. Enzymes ensure they proceed at the right time and place and with the right specificity and timing. Figure 8.3 shows the difference between an endothermic and exothermic reaction.

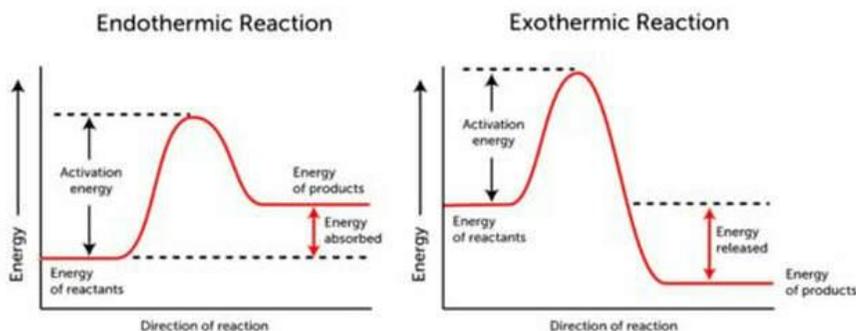


Figure 8.3. Endothermic reactions absorb heat (energy) and do not occur unless there is a catalyst and continuous energy input to keep the reaction going. Carrying water uphill to do work is an example of an endothermic reaction. More energy is expended than is captured. Exothermic reactions release heat (energy) and require a catalyst of some type to start the reaction. Each form of reaction, endothermic and exothermic, has an activation barrier. No reaction in your body occurs spontaneously, thankfully. Your brain controls all these reactions when and where they are needed.

Ultimately, even the action of enzymes comes from sunlight energy through photosynthesis and the resulting food or directly by the action of light waves on biological substances. The sun provides the power to activate the catalyst molecules through a complex chain of events. The work produced keeps your systems running and repairs the damage the work creates.

Think about the era before the industrial revolution. How did clever humans harness light energy to make their workload lighter? One such pathway involved evaporation. For example, the sunlight hits the earth and water in the ocean, raising the temperature and causing evaporation. Massive amounts of evaporation lead to rain. This water at higher elevations has potential (captured) energy that can be used later. Gravity pulls the water downhill. The water wheel, which turns some type of mechanism, can convert the energy from the sun into work.

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The wind is similar to, but less dense compared to, water. Our forebears used windmills to convert this sun-derived energy into work. A major use of this sun-induced wind work was to drive pumps to pull water up from aquifers to irrigate arid land. Now turbines are used to convert wind power to electricity directly. All wind energy comes from the sun.

In summary:

- All energy comes from the sun, which is derived from fusion. $E = MC^2$
- The energy comes to earth in weightless waves of light energy. $E = h\nu$
- Energy is light.
- Light is composed of waves.
- Photoreceptors of all ilk absorb light waves and convert them to different forms of energy we use.
- Coal, oil, natural gas, electricity, and wind all come from the sun's energy. In this respect, they are all renewable.
- Nuclear energy may be considered an exception. However, that is a discussion on how matter formed in the first place. Fusion is more fundamental than fission. We cannot use fissile that we have not fused into creation. And fusion is the primary process of stars.

Internal Temperature and Energy Usage

Our internal temperature is an indication of our constant need for energy. No one reading this wants to be at room temperature. That would mean you are not alive. Our internal temperature explains a lot about energy use and our health. Why do all humans have a body temperature that is roughly the same, 98° Fahrenheit (37°C)? According to Texas Wildlife, "No matter what the outside temperature may be, your body, like a living furnace, works to maintain a constant internal temperature. It generates heat by burning the food you eat. All mammals and birds can generate this internal heat and are called homoiotherms (ho-MOY-ah-therms) or warm-blooded animals. Normal temperatures for mammals range from 97°F to 104° F. Most birds have a normal temperature between 106° F and 109° F."²⁷⁸

Here are some excerpts from a scientific article attempting to explain body temperature. The key word is "attempting." "Scientists have found the reason why our body temperature is 98.6° Fahrenheit (37°C). Apparently, it is a perfect balance, as it is warm enough to prevent fungal infection but not so hot that we need to eat nonstop to maintain our metabolism."²⁷⁹ I find this sort of "reductionist" explanation inadequate and unscientific. They do not understand the expression about the chicken and egg or cart before the horse. However, this is the explanation of human core temperature that pops up first upon an internet search.

Let's do a quick dissection of this "science" before explaining the real reason our internal temperature is so stable and common to all humans and close to all other warm-blooded mammals.

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"Found the reason." Hmm. "The" is singular. That is not plausible.

"Warm enough to prevent fungal infection." Really!?! Do you think our creation and evolution of one of the most fundamental physiological conditions in our body revolves around fighting fungal infections? I believe our innate immune system takes care of that. And what came first, us or fungal infections?

"Not so hot that we need to eat nonstop to maintain our metabolism." This one is even more absurd. Our physical stature, activity, and baseline metabolism dictate our calorie needs. And the calorie content of the foods we eat determines how much we need to eat to meet those needs. Further, we have an elegant storage system for energy called glycogen and fat. So is it not quite obvious that the calorie content of available natural food and our metabolic needs are well matched so that we can easily adjust to eating just once a day or go much longer without food by fasting? And food, for the most part, is available at the right amount, time, nutrient, and calorie content to allow us to survive as a species. This is not coincidental - it is due to co-creation / evolution / adaptation.

Now for the real reason our internal temperature is stable and roughly the same from person to person. Genetically, humans are 99.9% the same, whereas we are genetically 15% different from rats. These genetic, thus metabolic differences explain the minor variations in core temperature between warm-blooded species. That we humans are all very similar explains why there is little variation in our core temperatures. So, what determines our core temperature and that of other warm-blooded species? It is the very basic science discussed above.

- Exothermic reactions occurring in our body release heat.
- Endothermic reactions occurring in our body absorb heat.

Sweat and skin surface area that transfers heat or cold to the environment is necessary to make minor adjustments to core temperature depending upon the physical activity and environmental conditions. However, exothermic reactions and endothermic reactions have the greatest influence, by far, on our internal temperature.

A balance within our physiology between exothermic and endothermic reactions determines our core temperature. Our genetic, thus, physiological similarities dictate that we are all driving the same reactions in roughly the same balance. And these are the reactions of human life that repeatedly occur, creating relative stability in our internal temperature. Moreover, even when we exercise, the balance between endothermic and exothermic reactions most likely remains relatively constant. Thus, our internal temperature is due to the summation of ALL reactions and not just some specialized set of processes that attempt to keep fungal infections at bay.

Consider this analogy.

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- A hot plate is plugged into an outlet and is heating up. This reflects the consequences of an exothermic reaction where energy is released.
- Also, water is dripped onto the plate to cool it down. The evaporation of water is the endothermic reaction. Energy is absorbed for the water to evaporate.

The balance between these two processes determines the final temperature. For example, if 10 of these test systems are set up and identical, the temperature of the hot plate surface will be the same.

I went to lengths to explain core temperature and the potentially complicated endo- and exothermic reactions because both these types of reactions are constantly occurring in our bodies. We do not have to consume energy - food - in the right form for all our cellular processes. Some foods we consume are ready to go to work - that is part of an exothermic or energy-releasing process. In other cases, the energy we get from food and light drives endothermic reactions. An example is that of melatonin and glutathione. It takes energy to prepare the anti-oxidant form of these substances. And expending energy for this process is a critical part of our energy-producing KREBS cycle. Energy must be expended to create even more energy. Reduction (anti-oxidation) of glutathione is an endothermic or energy-gobbling process, but it must occur for us to live and thrive.

Another example is taking a vitamin in a so-called "spent" form. Our body will expend energy to convert something "spent" back into something useful. Iodine and iodide are examples, too. Our body expends energy to convert iodide into iodine so that the iodine can perform the very specific work of oxidizing (killing) a pathogen, for example. Iodine is an electron stealer. When it steals from an infected cell, it kills the infection on its way to becoming iodide. The message here is to eat food, and your body will do what is necessary to put it to life-sustaining work in your body.

Energy from waves can be hard to appreciate because most of it is not felt. However, you can take your temperature and appreciate that you are consuming and producing energy. We can feel classical energies like temperature or kinetic energy. For example, if you stop suddenly by running into a wall, the force and its energy intensity are obvious. Another "container" for energy is oxygen in the air. It is produced by plants' respiration and is thus created from light waves (photosynthesis). Can you see the oxygen you breathe? You cannot, but your heart beats, and you can move your muscles. The invisible oxygen facilitates muscle contractions in both instances.

The point is, when it comes to energy in the form of the frequency of waves, you do not have to see it or even feel it for it to exert its force.

Light also contains magnetic energy. According to Washington University, "When the light gets into a material, it interacts with the charged particles within

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the atoms. Materials can absorb both magnetic and electric fields. The interaction of the field of light is usually about 10^5 (10,000) times stronger than that of the magnetic field. Thus, we can concern ourselves mostly with the interaction of the electric field of light with matter. When the electric field of light gets into a material, it causes the electrons to move."²⁸⁰ Remember, diseases are caused by the loss of electrons, while healing is affected by the gain. Magnetic fields of high intensity also produce electrons, and methods like pulsed electromagnetic frequency (PEMF) heal.

In the Western world, health is viewed as stemming from biology. However, it all starts with physics and chemistry, particularly light. Our bodies are exquisitely engineered energy-driven, and managed instruments. Our energy systems evolved in harmony with our anatomy, physiology, and environment over eons. Substances and cell emit, absorb, and responds to electrochemical signals in an extraordinarily complex and coordinated way. Therefore, energy medicine is more fundamental than biological medicine and should be an important part of any health intervention.

Types of Light Energy

Where does light energy go in our body, and what does it do? In general, there must be a match between the frequency of a photon or wave of light⁶ and the molecule it interacts with for it to be absorbed and have an effect.

Gamma-ray photons have the highest energy in the EM (light) spectrum, and their waves have the shortest wavelength. They are very similar but stronger compared to X-rays, which most of us have more familiarity. These photons can break apart substances with the ease with which they interact.

X-ray photons are highly energetic enough to break up molecules and damage living cells. When X-rays hit a material, some interact, and others pass through. This feature of X-rays allows for imaging, but not without some level of damage created to the tissue with which it interacts.

Ultraviolet (UV) light photons are not considered ionizing radiation, as are gamma and X-rays. However, UV light is critically important as it can damage and heal. DNA, for example, is a very large molecule that normally absorbs energy when interacting with UV light and then quickly converts or releases that energy in some manner. Thus, when UV light interacts with a substance, it adds energy sending it into an "excited" state. All systems try to return to a more stable ground state by shedding that energy.

⁶ Is a photon a wave? I use these terms interchangeably but physicists may disagree. It is all about quantum mechanism beyond the scope of this chapter.

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In some cases, bonds are broken, and the molecule is destroyed or modified. In other instances, heat or light may be given off. It turns out that DNA is extremely effective at dissipating the extra energy quickly, so it gets damaged less than 0.1% of the time interacts with UV light. However, this higher energy state also provides great benefits. When interacting with UV light, molecules in the skin can easily undergo chemical transformations. Examples are the formation of vitamin D and melatonin. But its action is probably much more profound than just this. UV light creates "free" electrons, and electrons heal oxidative damage.

Visible light photons are quite similar to that UV but have lower energy. Visible light does speed up reactions by elevating electrons to an excited state. At this higher energy level, they can do more work. This is called "potential energy." This is similar to raising a heavy object on a pulley. Now attach the pulley to another lighter object and let it go. The heavy object will fall, and the lighter object will propel upwards. That is what visible light does - it raises a molecule into a more reactive state so it can more easily be transformed into a new form of energy or give off its excess energy to some other substance.

The most fundamentally important action of visible light is on the chlorophyll molecule. Chlorophyll is found in virtually all photosynthetic organisms, including green plants, cyanobacteria, and algae. It absorbs visible light energy, which is then used to convert carbon dioxide to carbohydrates. Plant chlorophylls absorb mainly in blue (between 400 and 500 nm) and red (around 650 to 680 nm) visible light wavelengths. Without visible light and chlorophyll, there is no life on our planet.

Infrared light photons are the most abundant light energy from the sun. As we go to lower energy along the electromagnetic spectrum from visible light, the next form is infrared light. Whereas X-rays break apart molecules and the UV and visible light (photons) elevate electrons to a more energetic state in molecules, infrared light interacts by causing chemical bonds to vibrate. Motion is heat, and thus infrared light causes molecules to heat up. After all, temperature is defined as the average of the molecular motion of the particles.

If you want to get warmer in the winter, the solution is simple, make the air molecules go faster! Easier said than done. We normally rely on the earth to absorb infrared light and then radiate it back to the air as heat. When you feel the sun's warmth, it is infrared light, not the more energetic forms of the EM spectrum. That is, visible and UV light do not make you feel warm.

The strict definition of what infrared wavelengths do to molecules is the following. "Infrared radiation absorbed by molecules causes increased vibration. Collisions between these energized molecules and others in the sample, tissue, for example, transfer energy among all the molecules, which increases the average thermal energy and, hence, raises the temperature." Simply put, temperature is movement.

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In infrared light, bonds are not broken, and no electrons are elevated. However, in chemistry, and thus physiology, there is a fundamental concept called the activation energy explained above. For a reaction to occur, the activation energy must be overcome. This is a beautiful part of nature, as reactions do not just spontaneously occur. If they did, our world would NOT exist as we know it.

Chemists use a "rule of thumb" for how quickly a reaction will proceed. That is, how easily reactants obtain enough energy to get over the activation energy hump to form products. This "rule of thumb" is based on the average activation energies required to get molecules to interact. In general, for every increase in 10 degrees Celsius or 18 degrees Fahrenheit, the reaction rate doubles. Therefore, infrared energy matters. It speeds up reactions.

On your skin, infrared light supports the visible and ultraviolet light in converting molecules into new products like vitamin D and melatonin. Unfortunately, that is potentially bad news for those far from the equator, with low light intensity due to the angle between the sun and the earth's surface in those regions.

You are probably thinking; 18 degrees Fahrenheit is a big temperature change considering that normal body temperature is around 98°F and a high fever is 104°F. This represents an increase of just 6 degrees. However, enzymes reduce the activation barrier dramatically. Figure 8.4 shows the difference in activation energies needed to complete a reaction with and without an enzyme or catalyst. In this case, the enzyme reduced the activation barrier by about two-thirds. This translates to a reaction happening nine times faster in the enzyme reaction than without the enzyme. Even a two or three-degree increase in internal temperature, coupled with an enzyme-facilitated reaction, will lead to a doubling in reaction rate.

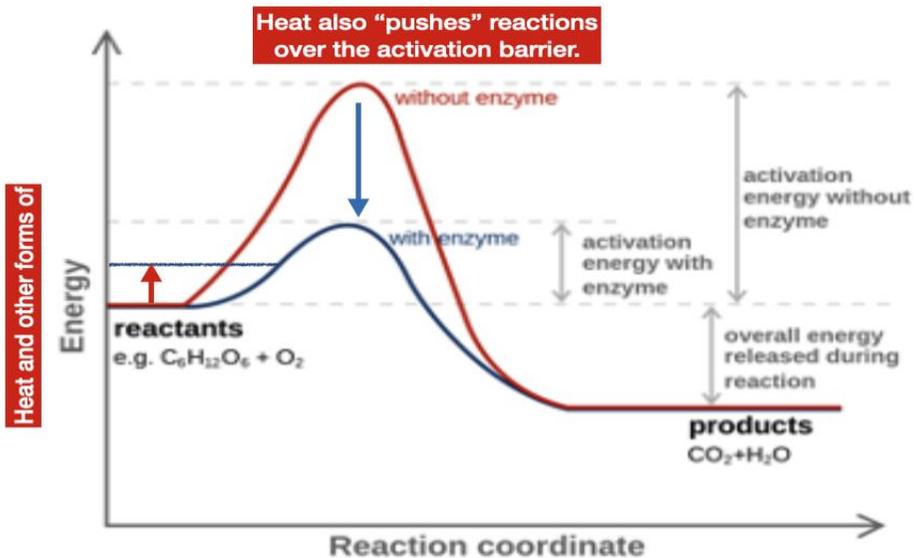


Figure 8.4: Comparison of a reaction with and without an enzyme. The enzyme-catalyzed reaction will go about nine times faster. Increasing the environment's temperature will cause the enzyme reaction to accelerate because the activation barrier is substantially lower, and the energy of the reactants is elevated.

In physiology, reactions run your energy and healing, so adding heat by any means, including red and infrared light, will increase your energy and shorten healing time.

There is not a sharp line of demarcation between infrared and visible light. Red light, the lowest energy visible light, provides some warmth, and near-infrared light, the closest to visible light in energy, provides some electrons. It all depends upon the energetic profile of the substance interacting with the light. To go further into this concept would require a detailed chemistry lesson which most people reading this do not want. Linus Pauling, the two-time Nobel Prize winner, was awarded the Chemistry Nobel Prize for his work on "the nature of the chemical bond."²⁸¹ Dr. Pauling's work provides vital insights into how our bodies work.

Did you know that our body glows? That is, it absorbs AND emits light.²⁸² This is fundamental to chemistry. Emitting heat upon an exothermic reaction is well understood. However, another pathway to release energy after a chemical reaction involving light is to release light. I enjoy the use of the term "glow." But it really means that our body is producing or releasing light energy just like it releases heat energy that keeps your body at approximately 98 degrees Fahrenheit. We are not exactly light bulbs, meaning that most energy we consume or absorb is converted into biological work or heat, not light.

That we produce light inside our body may signal inefficient energy use. On the other hand, it might also be a way to provide light energy deep into our tissue even when we are not exposed to sunlight. In chemistry, when light is shined upon a molecule, an "excited state" is produced that contains a transient "free" electron. If nothing picks up this electron, it "relaxes" to the ground state, releasing that energy. When light is one of the ways energy is released, it is of lower energy than the original light. As a result, there are energy losses as no process is 100 percent efficient, even within our bodies. The new wavelength of light noted in our glowing bodies may have important physiological consequences. For example, red light absorbed by a substance may emit infrared light needed in that specific area of our body.

Hopefully, you get the picture. We are energetic beings. Our internal temperature is mostly above ambient temperature, reflecting an input of energy and using that energy to create "work" or energy of some type - movement, for example. We "shed" some of that energy as perspiration to tightly regulate our internal temperature, but we also release some energy in the form of light. The point is we can interact with and produce the most basic form of energy - light!

Myths About Sunlight Being Harmful

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A substantial proportion of us who live in the industrialized world would benefit from more sun exposure. However, most of us are also reticent to do so or have lifestyles that limit exposure. Since energy is our being, we can interact with it to improve our physiology. Many people are worried about getting "too much" sunshine. They are worried about skin wrinkles or cancer. This is a mistake. Sun exposure can be greatly beneficial if the exposure happens based on the natural ebb and flow of sunlight. The way to obtain sun exposure above or below the equator is to go outside daily in the springtime, exposing as much skin as possible. Keep doing this, and your protective pigmentation will increase. By the time it is summer, your skin will be naturally protected.

There are two types of "skin" cancers: Skin cancers. These cancers are most commonly basal and squamous cell carcinomas that result from sun exposure on maladapted skin, and Cancer of the skin. In this instance, it is melanoma. There is a big difference.

According to the American Academy of Dermatology:

Basal cell carcinoma (BCC). This is the most common type of skin cancer. BCC frequently develops in people who have fair skin.

Squamous cell carcinoma (SCC). SCC is the second most common type of skin cancer. People who have light skin are most likely to develop SCC. However, if you are fair-skinned, you may be able to increase pigmentation through careful sun exposure.

Melanoma. It is often called "the most serious skin cancer" because it tends to spread. Melanoma can develop within a mole that you already have on your skin or suddenly appear as a dark spot that looks different from the rest.

Melanoma is a type of skin cancer that occurs when the pigment-producing cell, known as melanocytes, mutate and become cancerous. Even though invasive melanoma accounts for only about 1% of all skin cancers, it is responsible for the majority of deaths from skin cancer. Melanoma is dangerous because it is more likely to spread or metastasize than other skin cancers, such as basal and squamous cell carcinoma. Most pigment cells (melanocytes) are found in the skin; therefore, most melanomas are found on the skin's surface, such as on the back, neck, or legs. But melanoma can also occur in the nail bed (acral lentiginous melanoma), in the eyes (ocular melanoma), and on internal mucosal surfaces (mucosal melanoma), such as the lining of the sinuses, mouth, anal canal, or vagina. In addition, sound research shows that melanoma is not caused by sun exposure. In fact, incidences of melanoma go down with increasing sun exposure.²⁸³

Figure 8.5 shows all causes cancer mortality data vs. sun exposure. This image clearly shows that in areas of low sunlight, all-cause cancer mortality is substantially higher than in areas of high sunlight intensity. The notable exceptions are areas where people are more inclined to avoid wrinkles. These

include the bay and Los Angeles areas of California and along the Florida coast. In addition, past sunburns were actually associated with a decreased death rate from melanoma. Therefore, the increase in cancer deaths in these regions is due to sunlight exposure avoidance or excessive sunscreen use.

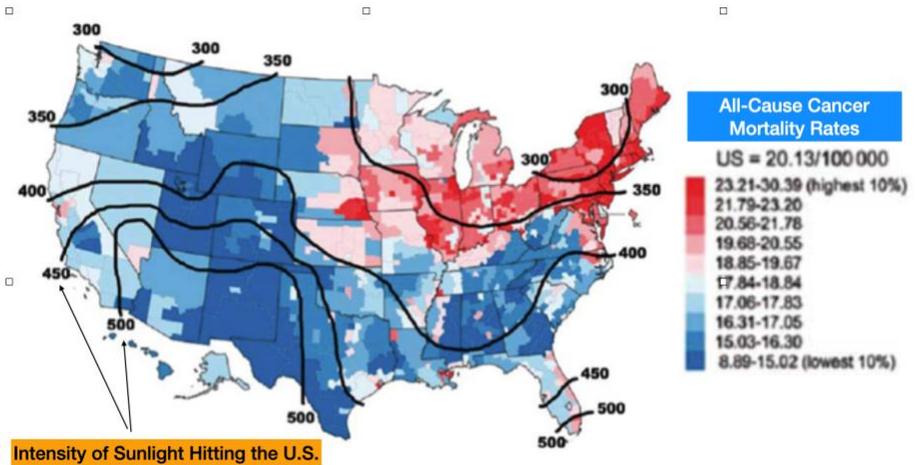


Figure 8.5. All-cause cancer mortality and sunlight intensity in the United States. Cancer death risk goes up as sun exposure goes down.

A compelling study on melanoma and sun exposure is titled "avoidance of sun exposure is a risk factor for all-cause mortality results from the melanoma in southern Sweden cohort."²⁸⁴ This was a very large study of about 30,000 women selected randomly and between the ages of 35 and 64. They were followed prospectively for 20 years, and there were about 2,500 deaths. Each lady filled out a detailed questionnaire emphasizing sun and light exposure, for example, from tanning beds. The study concluded "that avoiding sun exposure is a risk factor for all-cause mortality. Following sun exposure advice that is very restrictive in countries with low solar intensity is harmful to women's health."

A further finding was that the fair-skinned Swedish ladies who sought the most sun had a fifty percent lower death rate caused by melanoma than those who avoided sun exposure. These findings on melanoma death rates are completely consistent with all-cause cancer mortality rates, and the study cited here is just one of many corroborating these outcomes. As a result, Michael Holick, famous for his stance on obtaining sun exposure and elevating vitamin D, was thrown out of the Dermatology Society.²⁸⁵ However, Labcorp quotes his studies on vitamin D in every lab report where vitamin D is measured. So much for the standard of care and their associated medical societies!

How Sunlight and Infrared Light Improve Health

Americans are much less healthy than people from other developed nations. One contributing factor is the time we spend outside. The average American spends

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93 percent of their life indoors, with 87 percent being inside buildings and another 6 percent inside a vehicle. And, during that meager 7 percent of the time exposed to the sun, people are mostly covered up from head to toe or slathered with sunscreen. Sadly, the downward trend in sun exposure is matched by an equal and opposite trend in chronic diseases. My Godson is African American and lives in Massachusetts. His mom covers his skin completely with sunscreen during the three months he spends time outside. He receives no benefit from the ultimate source of energy - the Sun.

"Go out into the light and warmth of the glorious sun, you pale and sickly ones, and share with vegetation its life-giving, health-healing power.

- The Health Reformer, May 1, 1871

Many of us appreciate that going outside and being exposed to sunshine is a good way to produce vitamin Ds. The ultraviolet or high-energy light converts the cholesterol derivative to vitamin Ds. Yes, that is "Ds" with a plural, as the vitamin D produced on your skin is a mixture of multiple compounds instead of a single substance you get in supplemental form. It turns out that your skin, the largest organ in your body, directly harnesses light of various types to produce substances important for health. But your skin is not your only photoreceptor, as explained earlier. Your eyes are the most obvious photoreceptor. Essentially every molecule absorbs light. However, they absorb specific wavelengths or ranges rather than all light. Can you name another large photoreceptor on your body? The answer is in the footnote.⁷

Only recently has information emerged that infrared radiation from the sun directly stimulates the mitochondria to produce melatonin. It does so intracellularly and specifically within the mitochondria where oxidative stress from producing cellular energy is occurring. This is similar to the brain and cholesterol. Food and the liver provide cholesterol to the body. However, this molecule is so important to brain health that the brain provides a pathway to produce cholesterol. We are now learning that most of the melatonin in our body is produced inside cells.

Our body obtains the melatonin it needs in three ways:

1. At nighttime, in a dark environment, the pineal gland⁸ starts the production of melatonin. However, it is now believed that this process

⁷ Our ears and eyes gather and shape sound and light respectively. Just as the curved cornea of the eye angles light onto the pupil, so too the ear cartilage and ear canal concentrate sound onto the eardrum.

⁸ The pineal gland was commonly called the "third eye" for many reasons, including its location deep in the center of the brain and its connection to light via the circadian rhythm and melatonin secretion.

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only accounts for about 5 percent of the melatonin needed and used by our body. The melatonin produced in the brain has two purposes. The first is to send a "go to sleep" signal. The lack of light in the eyes also signals cortisol production to stop. The combination of low cortisol and high melatonin triggers sleep. Importantly, because we mainly sleep to repair our brains and eyes, the melatonin produced in the pineal gland plays a role in brain and eye cellular detoxification. Cholesterol is there to rebuild and repair damaged cells and build new cells. Thus, melatonin and cholesterol are the yin and yang of brain health.

2. **Supplementation.** Supplemental melatonin goes into circulation and provides it to the body generally. However, if taken during the daytime, it may signal a sleep response that conflicts with what the pineal gland is doing because it is still exposed to light. The light induces cortisol secretion through the suprachiasmatic nucleus (SCN) that activates the adrenal system.
3. **In the daytime, by the action of infrared light on mitochondria.** Melatonin is produced intracellular - that is, inside cells. This process is explained, in detail, later. Ninety-five percent of the melatonin in our body is produced in this way. Melatonin is produced in the daytime to manage oxidative stress from our activities. The melatonin produced at night time is insufficient to meet the needs of daytime anti-oxidation. Thus, this important additional mechanism for its production is crucial. Sunlight exposure is crucial. Without adequate intracellular oxidation damage repair, chronic diseases erupt.

How Melatonin is Produced in Cells During the Daytime.

Sunlight, particularly the infrared portion of light, penetrates deep into tissue stimulating the mitochondria to produce melatonin. As an intracellular oxidation regulator, it protects various diseases identified with mitochondrial dysfunction, including cancers, neurodegenerative diseases, cardiovascular disease, diabetes, and infectious diseases, including COVID-19. This is just a short list of conditions that can crop up when oxidation runs rampant inside cells. Chronic cellular damage is likely responsible for most, if not all, chronic conditions.

Sanitoriums have been used in medicine for hundreds of years to reduce the severity of challenging infectious diseases like TB and leprosy. Vitamin D production is part of the equation and is produced on the skin by the action of UV light. Vitamin D boosts immunity and protects us from infection. Melatonin cleans up the aftermath of the oxidative damage produced by cellular respiration. Also, infections, particularly those that are intracellular in nature, produce oxidative stress. This oxidation is also quelled by exposure to sunlight through melatonin production.

Many of us have preconceived notions about how our body interacts with light. Most of us understand visible light and that our eyes have photoreceptors that

convert the light into an electric signal. We also experience the warmth on the skin. How many people realize this is due to infrared light, not some artifact of the light we can observe with our eyes? Hopefully, many people understand that the skin has photoreceptors and that some interact with UV light to produce vitamin D.

I often ask people to name a third photoreceptor. Most people think for a while but do not come up with the most obvious answer. If you took the quiz, you know it is your ears. This is an important exercise to educate or remind people that light is made up of waves and that the light waves we "see" are a small part of the solar spectrum of light (waves). The word "waves" should be put at the end of the word "light" to continue to emphasize the concept of waves, in general, not just visible "light."

A photoreceptor does not have to be some elegant and complex structure. Essentially every chemical absorbs light waves of some type. However, there is a difference between just interacting with light waves and interacting in such a way as to elicit some type of measurable biological response. For example, when excited by light, some substances assume a higher energy state and then relax back into the "ground" state. This is similar to you standing up and then sitting back down again. Nothing really measurable happened except for a small expenditure of energy. On the other hand, specific photoreceptors, eyes, skin, and ears do something tangible when interacting with light waves.

What Light Does When It Penetrates Deep into Cells.

New science explains that photoreceptors may be much more ubiquitous than originally thought. Infrared light can penetrate deep into our bodies. Do you think it can do this without reason? It activates photoreceptors or specific molecules at the cellular level. Infrared radiation can penetrate bones and the crevasses in the brain and even reflect the light waves down deep into these caverns such that gray matter may be exposed to near-infrared radiation. Studies show that the symptoms of multiple sclerosis improve upon exposure to sunlight; this deep penetration provides part of the explanation.²⁸⁶

Sunlight energy of the infrared type plays an extremely important supporting role in cellular energy production processes. Sunlight acts on our cellular energy plants, the mitochondria, intracellularly within these organelles. These complex structures produce ATP, which is our energy currency. However, like a motor vehicle engine, producing energy without managing the processes that can lead to the biological equivalent of overheating may either slow or stop energy production. At a cellular, this "overheating" is oxidative stress. This process is detrimental to cells and tissue. Immune cells are cells too, and when they are "overheated" with oxidative stress, your body loses some level of immune protection, leading to various diseases.

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Our energy is produced by the KREBS cycle. Inputs into that process are carbohydrates, proteins, and fats. NADH, ATP, and GTP are outputs, with NADH being the most important initial product. These substances provide high-energy electrons. Flowing electrons is electricity. We can capture electricity to do work of some type, like moving a vehicle or cooking food. Thus, through the action of sunlight on plants, energy is created, and by eating food that captures this energy, our mitochondria can convert that initial sunlight energy to a usable form - electricity. In biochemistry, energy is not referred to as electricity. Instead, it is called the electron transport chain. These biological wires deliver the electron energy to make our microbiology work.

The NADH, at the top of the chain, holds the electrons that are then donated and cascade down the electron transport chain. NADH is electron-rich and is referred to as a "reduced" substance. To be useful, it gives up its electron to perform important biological work. This is why intracellular antioxidants are so vital. Many forward-thinking medical professionals understand that essentially all disease is the oxidation of cells and tissue. Thus, reducing agents - also known as antioxidants - fight disease. But it is not as simple as taking an antioxidant supplement. Key physiological antioxidants work through very specific rather than general pathways. Taking the wrong or too many antioxidants in supplemental form may do more harm than good. Trust your body.

Many forward-thinking medical professionals understand that essentially all disease is the oxidation of cells and tissue.

Melatonin and glutathione ensure that the NADH and other electron transport chain components get the electron rather than giving it up to oxidized byproducts of cellular respiration. Anything that breaks the electron transport chain forces your body to work on fewer cylinders. The final piece of this process is the delivery of the electron to the RIGHT electron acceptor, also known as an oxidant. That oxidant is oxygen. Electrons have potential energy like water at a high elevation. The oxygen is like a water wheel that can "accept" the oxygen and turn it into tangible work. When water spills onto the waterwheel causing it to turn, we can harness that potential energy and turn it into work. Anything that robs your cells of electrons stops or slows the waterwheel.

Melatonin promotes the activities of antioxidant enzymes while suppressing pro-oxidant enzymes. As an example, melatonin augments glutathione levels by stimulating its synthesis. Glutathione is an important antioxidant that is present in very high cell concentrations. In mitochondria, melatonin upregulates the activity of a major antioxidant enzyme, superoxide dismutase 2, leading to glutathione production.

Glutathione is recognized as the "master antioxidant." It is best referred to as a sentry antioxidant to protect the cellular energy production king. Ok, this title is a bit too long, but it emphasizes its action's specificity. Immunity is oxidative, and

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we do not want antioxidants interfering with this process. Glutathione, as an intracellular antioxidant with specificity, does not interfere with immunity.

Here is how light enters the picture. Melatonin, a very powerful antioxidant, and its partner, cytochrome c oxidase, affect the final process in the electron transport (electricity) chain. The electrons combine hydrogen, in the form of protons and oxygen, to produce water. Light energy plays an important role in this process. Notice "chrome" in the word "cytochrome." "Chrome" means light, and "cyto" means cell. The enzyme cytochrome c oxidase is excited with infrared light, increasing melatonin production inside the cell, thus facilitating energy and water production. And the superoxide dismutase 2 from melatonin produces glutathione.

Cytochrome c oxidase and melatonin are health heroes because of what they do inside cells. Melatonin is not just a regulatory agent for sleep. Most of the melatonin in our body is not produced in the pineal gland. Instead, it is produced in the mitochondria from the action of infrared light and does not fluctuate in concentration with the circadian rhythm. It, along with the glutathione produced from melatonin, keeps us from rusting from the inside out. Importantly, supplemental melatonin probably is counterproductive because it can stimulate sleep response without getting inside cells to clean up the byproducts of metabolism.

The action of melatonin derived from light exposure is summarized here:

- The absence of light stimulates the pineal gland to produce localized melatonin for sleep and to cleanse the brain and eyes during sleep.
- Light hitting the pineal gland through the eyes stimulates cortisol production to wake us up.
- Infrared light from the sun penetrates deep into tissue and cells and stimulates cytochrome c oxidase to produce melatonin
- Melatonin is a specific intracellular antioxidant, and it stimulates the production of the intracellular antioxidant glutathione. This occurs during the daytime because we are most active and produce the most energy with inevitable oxidative byproducts.
- These specific antioxidants ensure that oxidants do not neutralize electrons of the energy-producing KREBS cycle that do all the work in our body.
- The specific antioxidants, melatonin, and glutathione, do not interfere with the oxidative action of our immune system. The immune system acts separately to control infections.

Melatonin Production and Light Energy

Less than forty percent of the sun's energy comes to us as visible light. The largest energy contributor from the sun to the earth is infrared light that we sense as warmth on our skin. This is lower energy than visible light and is of a frequency

between 760 and 1400 nanometers. Visible light extends from 760 to about 400 nanometers. Fifty-four percent of all the energy coming from the sun is in the infrared spectrum. The red-light portion of the visible spectrum is closest to the infrared region and provides value to cellular processes. For example, many infrared lamps cast a noticeable red glow. This is a frequency region from 600 to 760 nanometers. Many healing LED lamps give off light at very specific wavelengths, usually 660 nm, observed as red light, and 830 nm infrared light, sensed as warmth but invisible to the human eye.

Do you have preconceived notions about the power of light, that is, its intensity? Since light is energy, it is important to understand the two parts of light in this regard. The first is the wavelength. The wavelength determines the energy a single wave provides compared to another light wave of a different wavelength. A short light wavelength contains more energy than a longer light wavelength. However, intensity also matters. You would probably not sense the exposure if exposed to one wave of high-energy UV light. However, if you were exposed to a high intensity of much lower energy light, 830 nm infrared light, you may experience a skin burn.

The term "lux" defines light intensity, whereas wavelength defines energy. The two go together. The definition of lumen and lux helps us to compare light intensities. One lumen is approximately equal to the amount of light put out by one birthday candle from a distance of one foot. A lux is the intensity of light delivered by 1 lumen on a square meter of area. A single lux is rather dim. The table below shows the light intensity from various sources compared using the lux scale. We are all more familiar with the term "wattage" when it comes to light intensity. Higher-wattage bulbs put out more light (lux) but have the same frequencies as lower-wattage bulbs.

LUX LEVEL	SOURCE
1	Twilight
5	Low street lighting
10	Low sunset
50	Room indoors with windows
100	Dark overcast day
320 - 500	Office lighting
400	Sunrise / Sunset
10,000 - 25,000	Full daylight
32,000 - 130,000	Direct sunlight

Table 8.1. The intensity of light delivered by the sun and lighting.

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Grasping intensities is important for health. The "dose" makes the cure. For example, to get going in the morning, sunrise light is much more intense than home lighting by about a factor of five. To raise your cortisol levels and increase morning energy, going outside is superior to inside lighting. Also, artificial lighting does not completely coincide with what hits the earth. We did not adapt to inside lighting, but we did adapt to the light delivered by the sun. The sun's light will wake us up, whereas room lighting behind low-E glass windows may not.

Many people interested in optimal health or healing are seeking light therapy. This is an excellent idea. However, human physiology is very complex, and it is naive to believe that one wavelength of light can heal. Most people seeking light as therapy are not going outside. Instead, they purchase LED panels, flexible wraps, and saunas that contain LED lamps and spend lots of money in the process. The better way is to go outside regularly, in the morning and during bright sunshine, to get the broadest exposure to UV, visible, and infrared light. Unfortunately, due to schedules and the latitude we live, getting adequate outdoor light is not possible for many of us. What is adequate light? Over 100 years ago, humans spent fifty percent of our time outdoors instead of the current seven percent. Can you increase your time outdoors by sevenfold? I did not think so.

****Important!** We have evolved and adapted to thrive in the light and the dark. How we interact with these two extremes is similarly important to health.

After investigating red and infrared light therapy for my personal use, I had an epiphany. Exposure to a few narrow bands of infrared light or just a segment of the infrared spectrum produced by LED bulbs may be helpful. Still, I project that it will be proven relatively ineffective compared to sunlight. There are alternative solutions for those who have insufficient sunlight exposure. However, only a few companies provide this solution.

The figure below explains my point by comparing narrow-band LED lights and halogen lamps to sunlight. The light emitted by halogen and incandescent lamps overlaps quite closely. Halogen lamps provide more visible and near-infrared intensity than incandescent bulbs. Also, incandescent lights of 500 watts are not available, but that wattage is readily available in halogen bulbs. Both provide a broad spectrum of light similar to sunlight. The difference between the incandescent and halogen bulb emission spectrum is not grossly different. Still, if you have a choice, halogens are more representative of what the sun delivers to earth.

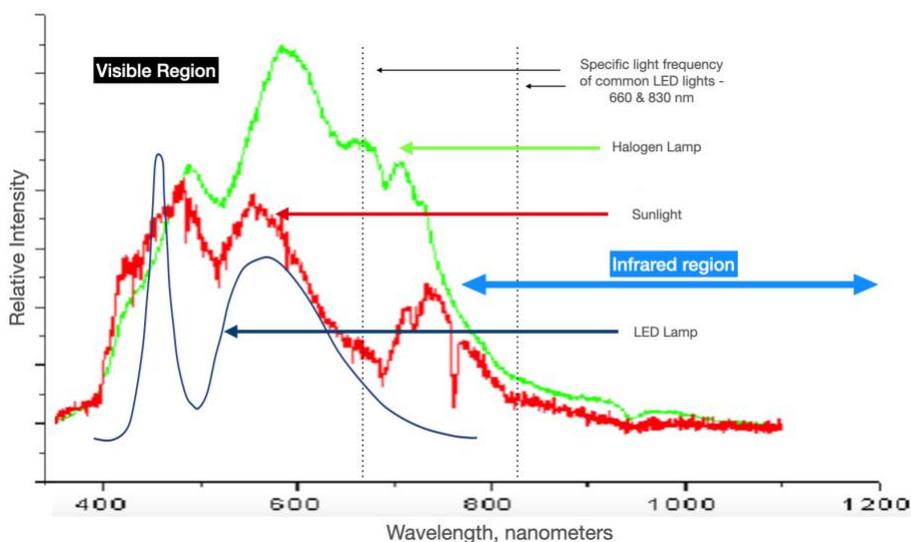


Figure 8.6 The spectrum of light emitted by the sun (red line), broad-spectrum LED light (dark blue line), and a conventional halogen bulb (green line). The two black vertical lines show the narrow frequencies emitted by certain LED lights used in infrared mats and saunas.

Do you think the light emitted by narrow-spectrum LED lamps (660 and 830nm) is somehow the "right" frequencies for all types of healing? Using LED lights of a specific frequency is woefully inadequate compared to the solar spectrum and problem less than optimal for comprehensive healing. Halogen lights are superior because of the similarity of the light they emit to the solar spectrum.

Figure 8.7 shows the absorption of cytochrome c oxidase in its oxidized and reduced forms. Since these "chrome" molecules absorb red and infrared light, the light source must overlap with the absorption profile of the molecule. If it does not, there is no interaction. Remember, cytochrome c oxidase provides electrons to the KREBS cycle.

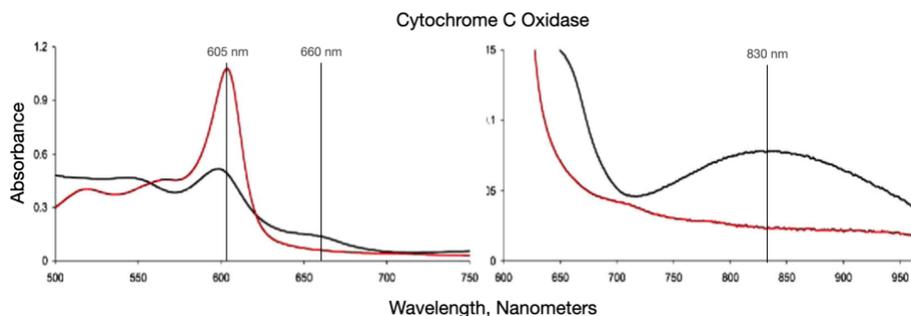


Figure 8.7. The absorption spectrum of cytochrome c oxidase. The red line is for the reduced (anti-oxidant) version, while the black line is for the oxidized version.

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The black vertical lines show the molecule's absorption at 660 nm and 830 nm, which coincides with light generated by infrared LED systems that are not broad-spectrum emitters. However, the maximum absorption for the cytochrome c oxidase molecule is at 605 nm, NOT 660 nm which is what LED lights output. At 660 nm, the absorption is low. The 830 nm light from LED sources matches the absorption profile of cytochrome c oxidase better. Still, the absorption band for the compound is broad, and the halogen lamp puts out much more energy through the entire absorption region of this compound.

If you want to enhance your KREBS cycle with light, sunlight and the light from a halogen bulb are superior to an LED light source.

Debate rages between the value of near-infrared vs. far-infrared saunas. Here is your answer as to which is best. Does the sun put out just near or just far infrared? This debate is a moot point. Mimicking the sun as your light therapy device is best. And the best source of light for that across the visible and infrared regions, if not the sun, is \$1 halogen bulbs. I conclude that the broad spectrum of light delivered by a halogen bulb is therapeutically superior to that provided by broad-spectrum and infrared LED bulbs.

Sunlight energy provides myriad health benefits, but reducing oxidation from energy production inside cells is at the top of the list.

Light, Darkness, and the Circadian Rhythm

Sleep may be as important to health as immunity and controlling oxidation inside cells. Without good sleep, your body does not repair and detoxify your brain and eyes well. In this sense, sleep and the repair and recovery associated with it are more fundamental to health compared to immunity. We need strong immunity when we are vulnerable, and sleep reduces our vulnerability to disease. Sleep and the circadian rhythm are affected by light. The conductor of all processes in your body - the master clock - is the circadian rhythm. Figure 8.8. shows the circadian rhythm. The breadth of what it manages goes well beyond falling asleep and waking up. Its impact is much more profound.

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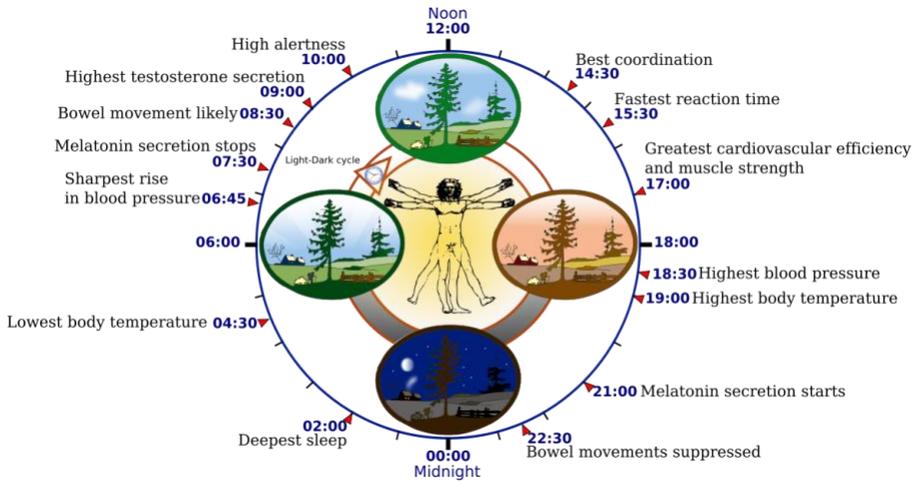


Figure 8.8. The impact of the circadian rhythm on human health.

The human body is extremely complex, and many processes are either ongoing or intermittent. Timing is everything, and our master clock regulates when key processes happen. Here are some key programmed events driven by light and darkness - your circadian rhythm, at least when it is operating normally. They run efficiently only when your sleep and awake time follows that of sunshine.

- 7 am: Melatonin stops being released;
- 7 am: Cortisol levels are elevated, and glucose shoots up to start your engines
- 10 am: Greatest alertness;
- 2:30 pm: Best coordination;
- 3:30 pm: Fastest reaction times;
- 9 pm: Melatonin produced;
- 9 pm: Cortisol levels at lowest levels.

Light must be eliminated around 9 pm to keep your circadian rhythm in synchronicity. The absence of light triggers the pineal gland to stimulate melatonin production in the brain. If this does not happen, the circadian rhythm will become misaligned, as will all associated processes. You might think this is no big deal as symptoms do not arise instantly. However, most of us who miss a good night of sleep often are not as sharp mentally, and sometimes we experience brain fog. Fighting against the natural rhythm dictated by the universe's flow impacts energy and health like a slowly growing cancer.

Obesity is a global problem, and it is assumed to be due to an intake of excess calories, specifically carbohydrates. However, your metabolism dictates the need for calories and nutrients, and the circadian rhythm controls your metabolism. Eating in windows outside of the earth's natural rotation puts your calorie intake out of sync with regulatory hormones like cholecystokinin, leptin, insulin,

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glucagon, and ghrelin. When you consume foods outside of the appropriate window, storage as fat is the result. When your body is in repair mode during sleep, it is like having your automobile in the repair shop. The engine is not on - at least fully, so calories taken in at that time are calories that become stored rather than used. Being out of sync with the circadian rhythm has a range of potential implications, including:

- Body temperature alterations
- Altered metabolism / weight gain due to metabolic hormone dysregulation
- Altered immune system function
- Tumor development
- General perturbations to hormonal homeostasis (body-wide regulation)
- increased markers of inflammation at the root of most chronic conditions
- Major chronic disease development, including cardiovascular diseases, cancer, Alzheimer's, and diabetes

Many people are now watching their glucose with continuous monitors. I very often hear that individuals have high glucose levels in the morning despite fasting, calorie restriction, or a keto/high-fat diet. The morning glucose levels have little to do with calorie intake. In the early morning hours, hormones, including cortisol and growth hormone, signal the liver to boost glucose production. The purpose is to provide energy that helps you wake up and get going.

I might be that rare person who advises not to use continuous glucose monitoring. They may help find an association between the intake of certain foods and glucose levels, but too many factors confound the information. And we already know what foods drive up insulin and glucose, so you really are not discovering anything new.

How to optimize metabolism is well understood. Ultimately, glucose is very important. However, like cholesterol, it has been inappropriately demonized. Instead, focus on your fasting insulin level. This hormone is regulatory, whereas glucose is not. Does getting on the scale every day help you when trying to lose weight? The same will be proven to be true with continuous monitoring devices. The point is constantly monitoring glucose does NOT provide information about your insulin sensitivity because its level is not always driven by what you have or have not eaten.

Circadian Rhythm Regulates Processes in Your Body

When light enters the eye, some of the energy goes to what are called intrinsically photosensitive retinal ganglion cells. From here, the signal created by the light is sent to the brain's suprachiasmatic nucleus, which is the master clock. That is the portion of the brain that makes sure everything is working in sync, like an orchestra conductor. In one instance, specific neurons that shut down melatonin production are activated in the pineal gland. This is an important step toward getting going first thing in the sunlit morning.

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Five percent of the population gets symptoms of seasonal affective disorder. Dozens of studies found that when affected people were exposed to very bright light in the morning at 10,000 lux (full sunshine) for about 20 minutes for four days, there was an improvement in seasonal affective disorder. The way to get this very high level of illumination is to go outside or turn on a bright halogen lamp first thing in the morning.

Seven thousand lux of bright white light versus fifty lux of dim red placebo light exposure in the early afternoon is correlated with improvements in bipolar disorders. Higher intensities showed corresponding better outcomes. Exposure to bright dawn light had a similar impact on this condition.

Many people feel sluggish in the morning and opt to stay in bed, shower, or reach for a stimulant. Instead, sound research shows that intense light exposure is a better and more natural way to start your day. Dawn sunlight improved subjective well-being, mood, and measurable cognitive performance compared to the dim light found indoors. Dawn stimulation with artificial solar spectrum light may be very helpful, particularly for those living far from the equator. This is not a weak light bulb but a rather intense light source that simulates the solar spectrum. The right source contains ultraviolet, visible, and infrared light. Glass filters some UV light, so being in your house or car does not have the same profound impact as unfiltered sunlight. UV light is important too!

Reestablishing a normal rhythm may take a while if your circadian rhythm is shifted due to working nights or staying up late.

A key nighttime tip is to simulate life before electricity. If lights are not completely extinguished, do avoid light that is high up in your visual field. Light hitting the photosensitive cells in your eye from above looks much more like mid-day than low light that simulates the sun setting. With the advent of fire came more activity after sunset. Campfires are usually below our visual field and cast mostly reddish-orange and infrared, not blue light. This is quite similar to the sunset with its orange glow. It is reasonable to surmise that our body sees a campfire as an extension of sunset. Also, your eye's photoreceptors are particularly stimulated by low levels of high-energy blue light from modern backlit electronic devices. However, this type of light is preferred in the morning so gaze into your phone in the am but not in the pm.

Energy matters, and the lower energy red light has less of an impact on photoreceptors that keep cortisol levels elevated. In this regard, blue blockers may help at night but lower cortisol during the day. They may be appropriate for people who hold blue light-emitting devices close to their eyes. In these instances, the intensity of blue light may cause harm to your retina due to its high energy content. The intensity of light diminishes precipitously when moved away from you. Intensity drops by the square of the distance from you. Thus, if you move your phone away from you by a factor of three, the intensity decreases by a factor of nine!

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Multiple sclerosis incidence is higher the further populations are from the equator. Sun exposure could affect brain volume in multiple sclerosis. We now know that infrared radiation can penetrate the skull and bathe the cerebral spinal fluid and brain tissue previously thought inaccessible to light. In addition, new studies show that the trend in multiple sclerosis is not strongly correlated to vitamin D levels produced by UV light. Thus, red and infrared light probably play a bigger role in curbing this disease. The mechanism, of course, is the scrubbing of free radicals of oxidation occurring in your mitochondria.

Vessel health is whole body health. People who live the longest have healthy blood vessels, particularly at the capillary level. Red and infrared light improves vessel health. The red light of 670 nanometers improves nitric oxide secretion and facilitates smooth muscle relaxation and flexibility.²⁸⁷ Ultimately, exposure to sunlight in the "red" region increases vessel diameter leading to better blood flow. That is, the health of vessels is improved, and blood pressure is better controlled. Eat your beets, and there is no need for nitric oxide-producing supplementation if you also spend time exposed to bright sunlight.

Sun exposure improves outcomes in severe melanoma. Sun exposure also reduces all-cause cancer mortality and all-cause mortality from any disease. For those who remain unconvinced about obtaining intense sun exposure, you can still benefit from parts of the solar spectrum, but only if you go outside. Near-infrared light, which supports cellular energy production, has high reflectance off of green leaves, trees, and grass. Therefore, you do not have to be in direct sunlight to experience the benefits of infrared and red light.

We are supposed to experience direct sunlight and have compensatory mechanisms to manage damage from light. That is why people who live closer to the equator have much more skin pigmentation. However, this benefit is lost in the concrete jungle of cities, indoors, or behind windows. Modern e-glass filters out UV and infrared light radiation. Figure 8.9 shows the reflection of infrared light.



Figure 8.9: Infrared light reflecting off trees as noted by the red coloration. Notice the lack of infrared light from the buildings in the background. Credit: Paolo Pettigiani

Sunlight waves are a treatment for COVID-19. And, now that we know the so-called vaccines are not a treatment, it is safe to say that sunlight exposure is superior to the "vaccines" for COVID-19. Why is sunlight superior to a "vaccine?" The answer is sunlight waves work to reduce the intracellular stress created by the spike protein or other components of the SARS-CoV-2 substance. The ACE II is a receptor for an enzyme that helps module oxidative stress. The spike protein can occupy and shut down this receptor, thus leading to increased concentrations of reactive oxygen species.

Those of our population with high background levels of disease, thus oxidative stress, are more vulnerable to this process, pushing them over the edge into severe disease and long-haul syndromes. The main mechanism is reactive oxygen species damaging cells, particularly endothelial (blood vessel) cells causing micro clots, as observed with the d-dimer test. This process leads to hypoxia and low total body oxygen saturation. The regrettable endpoint in medical care is a hospital visit, ventilator, and high probability of death. Noteworthy is that there is no sunlight energy in the ICU. The harsh fluorescent bulbs put out very little red and infrared light.

Ultraviolet light therapy is also important in COVID-19. A study on people from the United States, England, and Italy demonstrates that UV light in a region that does not produce substantial vitamin D reduced COVID-19 mortality.²⁸⁸ The authors posited that nitric oxide production from sun exposure played a role in reducing deaths. They did not include infrared light considerations in their study. They concluded, "Seasonal variation in environmental and meteorological conditions affects the incidence of many infectious diseases and may also affect COVID-19. Ultraviolet A (UVA) radiation releases cutaneous photolabile nitric oxide (NO), impacting the cardiovascular system and metabolic syndrome, both COVID-19 risk factors. NO also inhibits the replication of SARS-CoV2."

There is a symbiosis between different types of light energy. Excess amounts of ultraviolet radiation can cause erythema (sunburn) in the short term and photoaging and skin cancers in the long term. Interestingly, pre-exposure to infrared light radiation preconditions the skin, making it less susceptible to UV-B radiation damage.²⁸⁹ This is probably an evolutionary adaptation, as the atmosphere absorbs and scatters ultraviolet and blue light in the morning hours shortly after sunrise.²⁹⁰ This morning exposure to infrared radiation is a cue to prepare the skin for mid-day exposure to more intense ultraviolet radiation.

Pre-exposure to infrared light radiation preconditions the skin, making it less susceptible to UV-B radiation damage.

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Late afternoon exposure to decreased amounts of ultraviolet radiation may be a cue to initiate cellular repair of the UV-damaged skin. This is an important part of the workings of our internal clock. This information also points out that just a few short sun exposures during the day may have benefits but also come with added harm compared to those who get more continuous sun exposure.

The mid-Victorians of England, in the period centered around 1870, lived longer and much better compared to British people today. They had 10 percent of chronic conditions, and this was attributed to hard work and good nutrition. We can now add another factor to their good health - sunlight exposure. In the 1800s, people got about ten times the light we get today, including infrared light exposure.

Daily sunlight exposure morning, noon, and night is your best source for the healing power of light energy. However, the reduction of infrared exposure due to the filters in the modern glass shows a dramatic shift in the exposure ratio to visible and infrared light. You can transition "back to the future" by installing unfiltered halogen lamps for times when you are not outside all day long and in fall, winter, and spring in more northern latitudes. Figure 8.10 shows the reduction in sun exposure over the last two centuries and the change in the ratio of visible to infrared light we received today because our sheetrock caves contain infrared light-filtering glass.

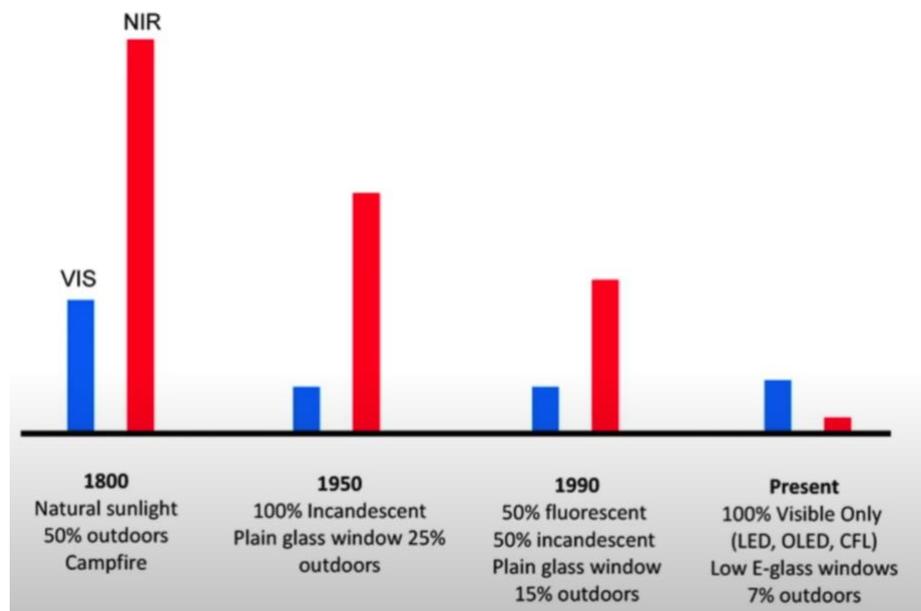


Figure 8.10. Changes in sunlight exposure over the past 220 years. Infrared light (red bars) contributes more energy to the earth than visible light (blue bars). Our modern lifestyle causes us to be inside and behind modern windows with infrared filters. This has shifted the exposure ratio to these two ranges of light frequencies.

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"The feeble one should press out into the sunshine as earnestly and naturally as do the shaded plants and vines. The pale and sickly grain blade that has struggled up out of the cold of early spring puts out the natural and healthy deep green after enjoying for a few days the health- and life-giving rays of the sun."

- The Health Reformer, May 1, 1871

The point the Reformer quote is missing is that all of us should press out into the sunshine, so we never become that "feeble one."

Other Modes of Energy Medicine

Energy medicine is not just that delivered by the sun. All energy does come from the sun. Other forms of energy medicine available at a clinical level include:

- Directed light therapy - low-level laser and LED therapy,
- Heat therapy - hyperthermia,
- Microcurrent therapy, and
- Pulsed electromagnetic field therapy, also known as PEMF.

Directed light as medicine

The two most common ways to deliver targeted light medicine are light amplification by stimulated emission (LASER) and light-emitting diodes (LED). The difference between them is that a laser produces coherent or specific waves of light while the LED produces a more scattered or broad spectrum of light. As a result, lasers can focus light energy into intense beams that can penetrate deep into tissues. However, certain frequencies of light experience less interference with tissue in the body and can penetrate more deeply, even at lower intensities. Near-infrared light contains such frequencies and is optimal for deep penetration.

Light-generating systems are classified numerically. The considerations for classification are:

- Laser light outputs energy or power;
- Radiation wavelengths;
- Exposure duration; and
- The cross-sectional area of the laser beam at the point of interest.

Classes define laser systems.

Class 1: This class is eye-safe under all operating conditions.

Class 2: This is for light systems that emit in the visible region (400-700nm). It is presumed that the natural aversion response to the very bright light will be sufficient to prevent damaging exposure, although prolonged viewing may be dangerous.

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Class 3: These devices may produce up to five times the emission limit for Class 1 or Class 2 lasers and, depending upon the subclass, have the potential to cause harm to eyes and other tissue.

Class 4: This is the highest class of laser radiation. These devices are always hazardous to view and may cause devastating and permanent eye damage. In addition, they may have sufficient energy to ignite materials and cause significant skin damage.

In general, the light from lasers and some LEDs is more intense than sunlight at the equator. However, since sunlight contains a broad spectrum of light, including high-energy UV light, it can damage the eyes.

Laser light of class 3B is most commonly used in tissue healing. However, a Class 3B laser produces high intensity light, so the maximum permissible exposure for eye exposure may be exceeded, and direct viewing of the beam is hazardous.

Cytochrome c oxidase, the light-absorbing substance inside mitochondria at the beginning of the biological chain that scrubs reactive oxygen species from cellular respiration, is stimulated to produce electrons at around 605 and 850 nanometers. This is in the red and near-infrared region of light. Modern lasers that are therapeutic produce intense light in these regions. The purpose of this specific light is two-fold. The first is to stimulate cytochrome c oxidase to produce melatonin and glutathione. The second reason is this wavelength range has the deepest tissue penetration through the tissue to reach cells. This is no coincidence. Critical physiological molecules like hemoglobin absorb light of shorter wavelengths than this range, and water absorbs longer wavelengths. Cytochrome c oxidase grabs the remaining light and can affect oxidative detoxification inside cells.

Lasers, with their intense, tight beams of light, can reduce oxidative stress inside cells, but this job is best left to sunlight that hits your entire body. However, lasers play an important role in repairing localized tissue damage. The red and near-infrared light stimulates gene expression activating growth factors. The light produced by these lasers stimulates a range of growth factors, including platelet, transforming, fibroblast, keratinocytes, and nerve growth factors, to name a few.²⁹¹ Light stimulates growth and repair factors in the human body, similarly to how it stimulates the growth of plants.

Near-infrared laser light directed at damaged tissue also increases angiogenesis and neovascularization.²⁹² This dynamic duo increases blood flow to the tissue that needs healing. Importantly, it is not just due to vasodilation. Instead, new blood vessels are formed to increase local circulation. "Neo" in neovascularization means "new." This implies stem cells are activated. Shining a near-infrared laser on adult stem cells derived from human body fat makes the stem cells replicate 54 percent faster.²⁹³ This process is surely going on locally in the body, induced by concentrated light therapy. The end result is an increase in

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muscle, cartilage, and bone regeneration and a decrease in inflammation and edema.

The defining work in localized near infrared therapy was performed at Harvard Medical School by Dr. Michael Hamblin. For those interested in learning more on this topic, consider reading "Mechanisms of Low-Level Light Therapy."²⁹⁴ The abstract of that article is reproduced here.

"The use of low levels of visible or near-infrared (NIR) light for reducing pain, inflammation and edema, promoting healing of wounds, deeper tissues and nerves, and preventing tissue damage has been known for almost forty years since the invention of lasers. Originally thought to be a peculiar property of laser light (soft or cold lasers), the subject has broadened to include photobiomodulation and photobiostimulation using non-coherent light. However, despite many reports of positive findings from experiments conducted in vitro, in animal models, and randomized controlled clinical trials, low-level light therapy remains controversial. This likely is due to two main reasons;

- Firstly, the biochemical mechanisms underlying the positive effects are incompletely understood.
- Secondly, the complexity of rationally choosing amongst many illumination parameters such as wavelength, fluence, power density, pulse structure, and treatment timing has led to the publication of several negative and positive studies. In particular, a biphasic dose response has been frequently observed where low light levels have a much better effect than higher levels.

This introductory review will cover some of the proposed cellular chromophores responsible for the effect of visible light on mammalian cells, including cytochrome c oxidase (with absorption peaks in the NIR) and photoactive porphyrins. Mitochondria are thought to be a likely site for the initial effects of light, leading to increased ATP production, modulation of reactive oxygen species, and induction of transcription factors. These effects, in turn, lead to increased cell proliferation and migration (particularly by fibroblasts), modulation in levels of cytokines, growth factors, and inflammatory mediators, and increased tissue oxygenation.

The results of these biochemical and cellular changes in animals and patients include such benefits as increased healing of chronic wounds, improvements in sports injuries and carpal tunnel syndrome, pain reduction in arthritis and neuropathies, and amelioration of damage after heart attacks, stroke, nerve injury, and retinal toxicity."

Get plenty of sun exposure daily to optimize your health and keep your internal engines running smoothly. To heal specifically damaged tissue, targeting the area

with concentrated waves of light is known to have some of the key benefits of sunlight.

Microcurrent Therapy

Healing involves the donation of electrons. Electrical therapy is a way to provide supplemental electrons to tissue.

There are two classes of electrical therapy. They are:

- Transcutaneous Electrical Nerve Stimulation (TENS), and
- Microcurrent Electrical Nerve Stimulator (MENS).

According to the Cleveland Clinic, there are two theories about how TENS works. One theory is that the electric current stimulates nerve cells that block the transmission of pain signals, modifying your perception of pain. The other theory is that nerve stimulation raises endorphins, the body's natural pain-killing chemicals. The endorphins then block the perception of pain. Either way, the benefits of this therapy on pain are vast. A list of conditions that respond to this therapy, as indicated by the Cleveland Clinic, are:

- Osteoarthritis (disease of the joints);
- Fibromyalgia (aching and pain in muscles, tendons, and joints all over the body, especially along the spine);
- Tendinitis (an inflammation or irritation of a tendon);
- Bursitis (inflammation of the fluid-filled sacs that cushion joints);
- Labor pain;
- Low back pain;
- Chronic pelvic pain;
- Diabetes-related neuropathy (damage to the nerves that connect the brain and spinal cord to the rest of the body);
- Peripheral artery disease (“hardening of the arteries” that circulate blood to the body).

Interestingly, peripheral artery disease is not a disease of pain. Therefore, there are probably healing benefits from this type of electrical current therapy besides modifying nerve signaling. This argues for the production of endorphins or electron donation, which may provide healing and pain relief.

Microcurrent therapy should be avoided for certain pre-existing circumstances, including pacemakers, implanted pumps, pregnant women, and people who have uncontrolled seizures.

Microcurrent stimulation uses electricity that closely mimics the electrical level of the body's cells. A TENS device uses milliamps current while microcurrent devices input microamps. A microamp is one thousandth the concentration of a milliamp. The current of the TENS device often elicits a noticeable sensation. However, the stimulation from a microcurrent device will often not be felt. The

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dose makes the poison and the cure. The "dose" of electric current differs between these two approaches.

Microcurrent therapy works because of its ability to stimulate cellular physiology and growth. In an important study dating back to 1982, this therapy was shown that could substantially increase ATP generation.²⁹⁵ Interestingly, increasing the current decreased the efficacy of the treatment concerning ATP production. Thus, MENS devices are now shown to outperform TENS devices in healing effects. This study also demonstrated the ability of MENS to enhance amino acid transport and protein synthesis.

MENS facilitates the availability of healing electrons through the electron transport chain. These micro-electrical currents are fundamental to life, energy production, and repair and recovery. However, pain is blocked at a high electric current, for example, delivered by the TENS device, but the current overload appears to have little effect on healing. Research has shown that microcurrent therapy is effective at increasing the level of ATP production substantially and cumulatively.

TENS: Best for pain

MENS: Best for healing

Some extra electrons are needed for healing because as cells are damaged, they become electrically imbalanced. As a result, the electrical current takes the path of least resistance through the body. In injury, inflammation generally means oxidation or a lack of electrons. This process either consumes or diverts some of the body's natural electron-producing (anti-inflammatory) processes. By either mechanism, the body's electrical current will bypass the injury rather than go through the injured area, and healing the damaged cells and tissue will take time. However, by applying electric current to the site of an injury, supplemental electrons are provided, and recovery will be accelerated.

Eye diseases have a tremendous impact on quality of life. This is because the eyes are an outcropping of the brain and what happens in your eyes often spreads to your brain. In general, there is about a ten-year lead time for the mechanisms that drive eye diseases to start impacting the brain. For example, glaucoma is estimated to affect 111.8 million individuals globally by 2040. Glaucoma is already a major public health burden internationally. Dr. Andy Rosenfarb produced an affordable microcurrent eye treatment based on technology established by German scientists decades ago. Dr. Rosenfarb refers to this treatment for various eye diseases, including glaucoma, as electro-acupuncture.

Electro-acupuncture combines traditional acupuncture with low-level electricity (through wires attached to the needles) to increase the stimulation to key acupuncture points around the eyes. This approach is useful for certain ophthalmic conditions involving severely impaired circulation and reduced optic nerve and photoreceptor nerve-cell activity. Dr. Rosenfarb has found that electro-

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acupuncture methods yield excellent results. Eye conditions that seem to respond favorably to electro-acupuncture include Retinitis pigmentosa (RP), dry age-related macular disease (AMD), Optic atrophy, Retinal detachment, retinal occlusions, normal-tension glaucoma, and lazy eye.

Electroacupuncture improves blood flow to the eye and stimulates the photoreceptors, optic nerve, and entire visual system by waking up dormant cells. It also stimulates the release of endogenous growth factors and stem cells which help the damaged and sick nerve cells repair and regenerate.

Dr. Rosenfarb developed specific ophthalmic electro-acupuncture protocols used in research studies at Johns Hopkins University and NOVA Southeastern University. His methods are evidence-based, and research verified improvement in vision in many cases. He teamed with researchers at Johns Hopkins University on the first-ever clinical study to determine the efficacy of treating Retinitis Pigmentosa with acupuncture and other traditional Chinese medicine therapies. The study, published in 2013, is titled "A pilot study of an acupuncture protocol to improve visual function in retinitis pigmentosa patients."^{296, 297}

Many conditions are improved with microcurrent. However, the published literature is not as comprehensive on these topics. They include:

Scar removal. Regenerative medicine doctors appreciate that organ removal and scars can disrupt electric signals. Thus, some people undergoing scar tissue removal with microcurrent see a reduction in pain remote from the treatment area.

Pain relief. In babies, pain is relieved compared to the standard of care for treating congenital muscular torticollis, a condition in which an infant's neck muscle is shortened, causing the neck to twist.²⁹⁸

Reverse migraines. A cellular energy crisis may trigger severe headaches. Lyme disease and related intracellular pathogens are frequently identified when tested in severe migraine patients. Infections are electron robbers, whereas microcurrents donate electrons.^{299,300}

Mood disorders. Does your doctor know how the most prescribed class of drugs - SSRIs - work? The answer is no, most likely. However, microcurrent therapy is well-documented to improve mood.³⁰¹ Electron stealers are understood to result in brain disorders as diverse as depression and Alzheimer's. Treponema and chlamydial infections are found in the plaques of Alzheimer's brains. As with migraines, electron donation therapy, affected with microcurrent, plausibly explains the relief often enjoyed by those suffering from depressive conditions.

Our microbiology expends substantial energy to create an electron transport chain to deliver cellular energy and mop up oxidative waste. Microcurrent therapy, as a source of electrons, has and will continue to show efficacy in treating a wide variety of acute and chronic conditions plaguing humans and animals.

Pulsed Electromagnetic Frequencies (PEMF)

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The earth naturally emits electromagnetic frequencies. Astronauts returning from space were fatigued and in pain, feeling lousy, and their bone density went down. NASA now places pulsed electromagnetic frequency devices implanted in space suits, and this simple tool improved the health of the astronauts. It turns out PEMF recharges the transmembrane potential of cells, increases ATP production, and increases the sodium-potassium pump's action. This pump pushes key nutrients into and drives waste out of cells. This process is a critical first step in internal cellular energy production. We have to perform work to get a benefit within our cells. This process does not just happen spontaneously. This pump requires energy, and PEMF is one form of energy that facilitates this task. Specifically, this pump increases cellular pH, reducing acidity, increasing oxygen uptake, lowering blood viscosity, improving circulation.

Simply put, PEMF improves energy and healing.

The specific mechanism of PEMF is the production of fibroblasts, increase in collagen synthesis, increase in blood vessel production (angiogenesis), and decrease in inflammation. An important area in which PEMF has been studied is wound healing. A study titled "Pulsed Electromagnetic Field Therapy Promotes Healing and Microcirculation of Chronic Diabetic Foot Ulcers: A Pilot Study" shows promising results using this modality.³⁰² The people in this study had very advanced chronic wounds. Importantly, to get a favorable response, the patients received multiple treatments of PEMF therapy (duration: 60 minutes; frequency: 12 Hz; intensity: 12 Gauss) for 14 sessions within three weeks. By the end of the treatment period, there was an 18 percent decrease in wound size in the active PEMF group compared with a 10 percent decrease in the control group. In addition, the PEMF group demonstrated a significant cumulative increase in cutaneous capillary blood velocity (by 28 percent) and a 14 percent increase in capillary diameter. In contrast, the control group showed a decrease in both capillary blood velocity and diameter.

Note 12 gauss is a low dose. Affordable PEMF devices have an output of up to 2000 gauss.

PEMF improves healing but also reduces pain. In post-op breast implant surgery, the pain was significantly reduced in the treatment group. Using a validated, subjective measure for acute and chronic pain, the pain experienced by those treated with PEMF decreased approximately 6-fold faster than those untreated. The treatment was 72 hours of intermittent PEMF therapy. Pain scores in those who were not treated were double those of the treatment group scores at 5 hours post-op and 8-fold higher at 72 hours post-op.³⁰³ The women in the trial who did not receive PEMF treatment thought they were treated, but a so-called "sham" device was used, making these data reliable.

Veterinarians use PEMF more frequently compared to medical doctors. Some documented healing processes involving PEMF therapy in animals include:

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- Ligament healing;
- Tendinitis treatment;
- Range of motion improvement;
- Repetitive motion injuries;
- Bone stimulation and regrowth; and
- Nerve regeneration.

PEMF is used mainly by chiropractors and veterinarians for function and pain. However, the underlying benefit of this therapeutic approach is an increase in general and local blood flow. The 1998 Nobel Prize in Physiology and Medicine was awarded jointly to North American scientists Dr. Robert F. Furchgott, Louis J. Ignarro, and Ferid Murad for their discoveries concerning "nitric oxide as a signaling molecule in the cardiovascular system." We now understand that this miraculous gas leads to a cascade of events that improve the health of the endothelium (blood vessels). PEMF increases local nitric oxide levels, blood flow, and vessel health.³⁰⁴

The production of nitric oxide may be the most profound benefit of PEMF therapy. A paper titled "The impact of pulsed electromagnetic field therapy on blood pressure and circulating nitric oxide levels: a double-blind, randomized study in subjects with metabolic syndrome" explains this observation. This therapy will likely have more noticeable therapeutic benefits in those with more severe circulatory issues and low nitric oxide levels. The results of the study are provided here:

- PEMF demonstrated an increase in NO after therapy, but SHAM did not.
- During exercise, PEMF reduced peak systolic BP but not SHAM.
- Subjects with resting hypertension (Systolic BP ≥ 140 mmHg) had significant reductions compared to SHAM.

Conclusion: PEMF may increase plasma NO availability and improve BP at rest and during exercise. However, this beneficial effect appears to be more pronounced in subjects with existing hypertension, at least in this study.

Some people experience benefits from PEMF, while others do not. The most likely explanation is the variation in the dose of the PEMF energy. Two factors are involved: 1. the time on the device, and 2. the intensity of the magnetic field in gauss. For example, the most popular PEMF mat device provides an intensity of 1 gauss. However, the Earth's magnetic field intensity is roughly 25,000 - 65,000 nT (0.25 - 0.65 gauss). Therefore, this device barely provides more energy than we all experience by being on planet Earth.

We treated a woman who had been partially ambulatory for ten years from an auto accident. She was treated on five consecutive days with a 200-gauss PEMF unit for two hours daily. The electrodes were placed directly on the back of her neck. As a result, she experienced substantial pain relief and a return to full

motion. At the end of the therapy, she exclaimed that her neck was back to normal, as was her life.

Energy Medicine in Molecular and Cellular Communication

How do molecules and cells communicate? If you have an infection, how does your body know about it and send substances to kill the infection and control the inflammation? Fibrinogen is a signal molecule. It recruits Fibrin to go and stitch a wound. How does fibrinogen get its signal and pass it along to ensure Fibrin is notified?

Electromagnetic interaction is the emerging model for how communication occurs within biological systems. When something can vibrate in the vicinity of a receptor, it creates co-resonance in the molecule receiving the signal. That is what turns it on to perform a response of some type. Think about a tuning fork of a specific design that puts out a narrow frequency. If a tuning fork of the exact same design is in another room, it starts vibrating when the first one vibrates. Cellular communication may work on precisely the same principle.

Scalar Energy Healing

Nikola Tesla invented machines that proved the existence of Scalar Energy. He found two energies in the universe: electromagnetic, broadly accepted and recognized, and Scalar. Tesla considered Scalar Energy as standing energy or universal waves that could be collected without any cables or wires. He believed these waves are a primal force in nature and that Scalar waves expand outwards in circles of energy. Albert Einstein acknowledged the existence of a scalar field.

Nikola Tesla may have been the father of scalar energy, but he was not the only person to discover its existence. Thomas Galen Hieronymus built some unusual electrical devices for his neighbor, Dr. Planck. Later, he discovered that the devices were radionic instruments,⁹ first introduced to the world by Dr. Albert Abrams of San Francisco. This sparked his interest in radionic technology and set his mind on learning more.

In 1949, after researching and building his device, Hieronymus became the first person to patent a radionics machine successfully. He believed that his device detected a previously unknown form of energy emitted continuously by all elements.

Once calibrated, he found that he could use the device to identify unknown mineral samples. The circuitry in this device utilized both electrical and optical components. When the patent official requested that the energy harvested have a

⁹Radionics is a system of alternative medicine based on the supposition that detectable electromagnetic radiation emitted by living matter can be interpreted diagnostically and transmitted to treat illness at a distance by complex electrical instruments.

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name, Hieronymus thought of two words that pertained to his device: Electricity and Optics. Rather than using both, he combined them, creating the term, Eloptic Energy.

Little did Hieronymus know, Tesla had already discovered and named it Radiant Energy, which would later be renamed Scalar Energy by the nuclear engineer Tom Bearden. Hieronymus demonstrated that electromagnetic energy can be converted into scalar energy and vice versa. This conversion explains how scalar energy works in human physiology.

The reported benefits of scalar energy treatment overlap with energy treatments involving measurable electrical or magnetic fields.

- Repairs DNA;
- Protects cellular DNA from damage by increasing the energy of hydrogen bonds that hold DNA together;
- Stimulates cell growth in human immune systems;
- Improves cell wall permeability;
- Supports communication between cells;
- Charges the mitochondria, the energy center of our cells - presumably with electrons;
- Inhibition of Cancer cells.

Hyperthermia and Fever

Fever is a natural immune response to harmful and life-threatening infections. Conversely, blocking fever can be deleterious because fever evolved as a defense against infection. Fever works by causing damage to pathogens and infected cells while sparing healthy cells.

Many potential pathogens can survive and function over a wide range of temperatures cooler than their optimum. However, temperatures slightly higher than the optimum can damage infectious species. Some modes of action include proteins, enzymes, membrane lipids, RNA, and DNA. Specifically, hyperthermia disrupts DNA synthesis in the cells of pathogens and "host" cells.

Fever may create equal harm to pathogens and healthy tissue, at least in the short term. However, our tissues have repair and recovery pathways that are part of our physiology. Pathogens do not have this ability. Instead, they depend upon replication to proliferate. When a single cell in our body is destroyed from hyperthermia, disease, or even exercise, it is repaired or replaced. When a single pathogen is destroyed, it loses all ability to sustain and repair. Also, our tissue does not signal an attack response from our immune system, but pathogens do.

In the case of pathogens, if they can "hide" from immunity or hyperthermia, they survive or thrive through replication. But this is seldom the case. Root canals are an example of an area where pathogens can "hide" and then replicate there and spread and replicate elsewhere. Also, hyperthermia-induced artificially rather

than through a fever may not globally increase body temperature. In this instance, the pathogen "escapes" the impact of the internal temperature change.

Thus,

- If our tissue is damaged or destroyed by fever/hyperthermia, it will be repaired.
- If a pathogen is present, fever or hyperthermia will reduce its population.
- Immunity will also reduce pathogen populations.
- Pathogens tend to be more susceptible to fever/hyperthermia.
- If the pathogen burden is sufficiently reduced, the immune system can control or eliminate it.

According to Scientific American,³⁰⁵ "Fever is an elevated temperature of the human body that is substantially beyond the normal range. Normal body temperature fluctuates daily from about one degree below 98.6 degrees Fahrenheit to one degree above that number. Lower body temperatures usually occur before dawn; higher temperatures occur in the afternoon."

However, even a slight increase in temperature, especially at nighttime, may indicate a low-grade chronic infection. Night sweats signify a slightly elevated nighttime temperature as this is the time when core body temperature is below the normal value. Chris Wilson, M.D., surgeon lieutenant of the Royal Navy, describes his long journey with Lyme disease in an article titled "my years with Lyme disease."³⁰⁶ He stated, "Constant pain, feeling permanently hung over, being unable to stand properly, and soaking erstwhile sleep partners, courtesy of night sweats, did not augur well for relationships."

Tuberculosis (TB) is historically known to cause night sweats. It is an ancient disease that has affected mankind for over 4,000 years.³⁰⁷ It is a chronic disease caused by the bacillus *Mycobacterium tuberculosis* and spreads from person to person through the air. TB usually affects the lungs but can also affect other body parts, such as the brain, intestines, kidneys, or the spine. Symptoms of TB depend on where in the body the TB bacteria are growing. For example, pulmonary TB may cause symptoms such as chronic cough, pain in the chest, hemoptysis, weakness or fatigue, weight loss, fever, and night sweats.

Scientific American further explains that "the hypothalamus, which sits at the base of the brain, acts as the body's thermostat. It is triggered by floating biochemical substances called pyrogens, which flow from sites where the immune system has identified potential trouble to the hypothalamus via the bloodstream. Some pyrogens are produced by body tissue; many pathogens also produce pyrogens. When the hypothalamus detects them, it tells the body to generate and retain more heat, thus producing a fever. Children typically get higher and quicker fevers, reflecting the pyrogens' effects on an inexperienced immune system."

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However, this temperature regulation is not what causes our internal temperature to be "normal." Our physiological reactions are what set our internal temperature. The hypothalamus works to regulate our normal temperature. Sweat is most likely the regulatory system initiated by the hypothalamus. Thermoregulation of body temperature is a more complex interplay between physiological reactions. It is a balance between heat production and heat dissipation. Heat is generated or absorbed internally as a byproduct of any metabolic process. Heat absorption is an endothermic process, while exothermic processes cause heat production. The balance between these two reaction types set the core body temperature of approximately 98.7°F

Fever can help fight infection, but sometimes it can climb too high for the body's good. For instance, internal body temperatures above 105 degrees °F expose proteins and body fats to direct temperature stressors. This heat distress can threaten the integrity and function of proteins accustomed to the body's usual temperature variations and low-grade fevers. As a result, cellular stress, infarctions, necrosis, seizures, and delirium are the potential consequences of prolonged, severe fevers.

The receptor environment at the hypothalamus is designed to put limits on fevers. In rare instances where the hypothalamus malfunctions, the result is typically low body temperature, not elevated.

The fever never occurs in isolation from other immune responses. In this sense, it is symbiotic. Higher temperatures speed up reactions. One type of reaction is the production and action of "acute phase reactants" that are part of innate immunity. Therefore, fever provides three benefits:

1. Temperatures above normal are hostile to the survival of pathogens.
2. Elevated core or localized temperatures speed up physiological reactions, including those associated with immunity.
3. Higher body temperatures reduce blood viscosity and provide more blood flow.

Focal Infection and Focal Temperature

Chronic infections cause many chronic diseases. Those chronic conditions localized to specific tissue are caused by "focal" or localized infections. The temperature to which pathogens at the infected site are actually exposed is currently unknown.^{308,309} However, it is almost certainly higher than that of the blood entering the infected site since heat is generated at the inflammatory site. For example, studies assessing the temperature of inflamed atherosclerotic plaques have found temperatures up to 4°F higher than core temperature.³¹⁰ Sources of localized heat include,

- Macrophages in inflamed plaques.³¹¹

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- Neutrophils activated to kill pathogens generate substantial heat.³¹² In addition, the oxidative reactions that produce reactive oxygen species generate this heat.
- Activated blood mononuclear cells, including lymphocytes and monocytes, generate heat.³¹³

Surprisingly high physiological temperatures of up to 50°C (122°F) are generated very locally. This was elucidated by measuring mitochondrial temperatures using temperature-sensitive dyes.³¹⁴

High Infection Rate at Lower Temperatures

An area with an exceptionally high infection rate is the sinus. U.S. adults with diagnosed sinusitis are about 30 million, or 12% of this population. In addition, the number of people with a constantly runny nose or the "sniffles" is substantially higher. At least two factors drive this nasal "pandemic." 1. The nasal cavity is cooler than other tissue because of high airflow from the cooler ambient air, and 2. the oral cavity close to the sinus often suffers from low-grade chronic infections. The following clinical testimonial provides context to this issue:

"My bloodwork revealed an underlying infection of some kind. I was recommended the MyPeriopath, on the hunch it could be a mouth infection. I did that and had some harmful pathogens in my results. I found a new dentist in my area that includes cone scans, and low and behold; they found an infection in tooth #15 on the top. It had a crown from many years ago but had NOT had a root canal. The infection is pretty bad and even pushed into my sinus. Crazy, considering I have had zero pain in that tooth or sinus."

Nasal hyperthermia irrigation dramatically reduces rhinitis.³¹⁵ Local nasal hyperthermia or inhalation of heated water vapor is a home remedy for various rhinitis disorders such as the common cold and allergic rhinitis. Inhaled heated vapor treatments and saline solution nasal irrigation reduce the effect on inflammatory mediator production in nasal secretions.

"Treatment of perennial allergic rhinitis by local hyperthermia" is a study demonstrating the value of hyperthermia.³¹⁶ The authors state, "Due to the cooling produced by airflow, the temperature of nasal turbinates¹⁰ varies between 88 and 95°F. This low body temperature range enables the development of rhinoviruses, the main agents of the common cold." Ninety-five patients with documented perennial allergic rhinitis were treated with local hyperthermia of the nasal passages in a formal clinic trial. Treatment and results were,

¹⁰ Turbinates are small structures inside the nose that cleanse and humidify air that passes through the nostrils into the lungs.

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- One series of three 30-minute insufflations of humidified air at 109°F was applied at two hr. intervals.
- In the active treatment group, patients were free of symptoms: one week after treatment, 75%, and one month after treatment, 68%, respectively.
- In the placebo group, patients were free of symptoms after treatment: at one week, 28%, and at one month, 17%.
- The placebo group experienced the same device but with room-temperature air.

This important experiment from 1982 clearly shows that hyperthermia alone, without fever and the associated immune response, is a safe and effective treatment for allergic rhinitis and, by extension, other temperature-vulnerable pathogens.

Fever

Donohoe Chiropractic weighs in on the value of a fever not lowered with antipyretic treatment.³¹⁷

- The rising body temperature kills many microorganisms and curbs the growth and replication of others. This is because viruses and bacteria grow best at temperatures lower than the human body.
- Higher body temperatures decrease blood serum levels of iron, zinc, and copper, all of which are needed for bacterial replication. As these minerals are reduced in the bloodstream, bacteria are starved.
- Increased temperature causes lysosomal breakdown and auto-destruction of cells, thus preventing viral replication in infected cells.
- Heat increases white blood cell formation and motility, thus facilitating the immune response. As a result, the white blood cells, which destroy the invaders, get where they are needed faster and do their job more efficiently.
- Phagocytosis (cellular clean-up) is enhanced, and the production of antiviral interferon may be augmented.

Donohoe illustrates that reducing fever is often harmful. A study of adults with colds found that aspirin and acetaminophen suppressed the production of antibodies and increased cold symptoms. In addition, these adults tended to have longer infectiousness. In a study of children with chickenpox, acetaminophen prolonged itching and the time to scabbing compared to placebo treatment. In test-tube studies, therapeutic levels of aspirin suppressed the ability of human white blood cells to destroy bacteria. Another study found that a host of pain relievers, including aspirin and ibuprofen, inhibited white-cell production of antibodies by up to 50 percent.

Although fever and sickness symptoms are regulated in different brain regions, both are inhibited by antipyretic drugs (e.g., NSAIDs and acetaminophen).

However, NSAIDs, particularly ibuprofen, have more anti-inflammatory properties than acetaminophen and may carry additional risks of promoting infection.³¹⁸

On the flip side, fever is beneficial in patients with meningitis. Notably, a fever greater than 40°C did not indicate a poor prognosis, but all children presenting with hyperthermia died, according to one study.³¹⁹

Many peer-reviewed reports show how reducing fever worsens outcomes. A sample of these studies includes:

- Sickness behavior in feverish children is independent of the severity of the fever - an observational, multicenter study.³²⁰
- Non-steroidal anti-inflammatory drugs, pharmacology, and COVID-19 infection.³²¹
- A study from Japan found that the frequent administration of antipyretics to children with bacterial diseases led to the worsening of their illness.³²²
- A Finland study of 102 children with salmonella gastroenteritis showed a significant negative correlation between the degree of fever and the duration of excretion of organisms.³²³ Children with a fever greater than 40°C had the shortest duration of bacterial excretion, whereas those without fever had the most prolonged duration. Fever has a favorable influence on the length of the infectious disease.

This review article provides many illuminating facts.

"Non-steroidal anti-inflammatory drugs (NSAIDs) have an optional prescription status that has resulted in frequent use, particularly for the symptomatic treatment of fever and non-rheumatic pain. However, in 2019, a multi-source analysis of complementary pharmacological data showed that using NSAIDs in these indications (potentially indicative of an underlying infection) increases the risk of a severe bacterial complication, particularly in lung infections."

"First, the clinical observations of the French Pharmacovigilance Network showed that severe bacterial infections can occur even after a short NSAID treatment, and even if the NSAID is associated with an antibiotic."

"Second, appropriate studies that overcame bias converged and confirmed the risk.

"Third, experimental in vitro and in vivo animal studies suggest several biological mechanisms, which strengthens a causal link beyond the well-known risk of delaying the care of the infection (immunomodulatory effects, effects on *S. pyogenes* infections, and reduced antibiotics efficacy)."

"Therefore, in case of infection, symptomatic treatment with NSAIDs for non-severe symptoms (fever, pain, or myalgia) is not recommended, given a range of clinical and scientific arguments supporting an increased risk of severe bacterial complication." ³²¹

JianFeng Chen works at China's Shanghai Institute of Biochemistry and Cell Biology. His team studied how immune cells travel from a blood vessel to the site of an infection. His team found that a fever gives the cells a superpower that speeds up that trip.³²⁴ How does this work? Increased temperatures reduce viscosity allowing for more blood flow. This is in addition to the antibiotic effect of the elevated temperature and the recruitment of immune cells. The Chen group also showed that T lymphocytes, the viral killer cells of the immune system, become produced at higher levels during fever and infection.

Hyperthermia Treatment and the Sun

Sunlight will increase core body temperature. Infrared light, the most abundant form of light waves in sunshine, increases the temperature of any substance with which it interacts. That is why you feel a tremendous warming effect from sunlight. The primary mechanism is surface and internal heating caused by the infrared light and not from warm air interacting with your skin.

Sanatoriums are well known for their healing benefits. These facilities are usually situated high in the mountains where sunlight, including warming infrared light, is not attenuated by the dense atmosphere's lower levels. H. I. Bowditch argued for the curative powers of "pure air and sunlight," recounting the story of a 30-year-old woman he had treated for tuberculosis. "We directed that she should sit out on this piazza every day during the winter unless it were too stormy," he wrote. "The balmy influences exerted on her by the daily sun and air bath was so grateful her breathing became much easier after each of them."³²⁵

Fever vs. Hyperthermia

Fever and hyperthermia share many mutual benefits. Fever may be superior to an artificially induced elevated core temperature mainly by recruiting more immune cells. Importantly, fever is self-limiting and well-controlled. With fever, unlike hyperthermia, body temperature is well regulated by a hypothalamic set-point that balances heat production and loss. Natural fever regulates temperature that will not climb relentlessly and does not exceed an upper limit of 42°C (106.7 F).

Fever seldom causes harm, especially long-term damage. Fever does not frequently exceed an upper range of 40°C (104°F), a temperature proved not to be injurious to tissue. Children, when sick, often run a higher temperature compared to adults. About 20% of children seen in the emergency room have temperatures over 40°C, and they usually make a full recovery. If there is morbidity or mortality, it is due to the underlying disease. The associated fever may well be protective.³²⁶

Hyperthermia as a treatment is well studied but seldom applied. A PubMed search reveals 44,000 medical peer-reviewed publications that include "hyperthermia" in the title. There is even a journal on hyperthermia titled "the international journal of hyperthermia. Most hyperthermia studies are on Cancer therapy. Also, in most instances, elevation in temperature is induced locally, for example, just in the tumor area. In these instances, the local temperature is substantially higher than that produced by fever. A better approach to matching what happens in a fever is to induce an elevated core temperature globally.

"Hyperthermia: How Can It Be Used?" is the title of a representative article.³²⁷ The authors state, "Hyperthermia (HT) is a type of cancer treatment along with surgery, radiotherapy, chemotherapy, and gene and immunotherapy. In oncology, HT uses an external heat source to increase tissue temperature, kill cancer cells, or impede their growth. The term 'hyperthermia' applies to several heat application techniques that are implemented in addition to other cancer treatments (particularly chemotherapy and radiotherapy)."

"There are three types of HT treatment predominantly used to treat cancer. Each requires applicators in contact with or in the patient's proximity for heating. Heating can be achieved using different types of energy, including:

- microwaves;
- radio waves; and
- ultrasound."

"However, the energy source will depend on the cancer type and location. The temperature used will also vary. HT is rarely used alone and can be combined with other cancer treatments. When combined with other treatments, improved survival rates have been observed."

"High temperatures, as most studies revealed, cause direct injury to cancerous cells and sensitize the cells to other treatment modalities, and augment radiation and chemotherapy with minor or no injury to normal tissues. Hence, HT is generally used as an adjuvant treatment for cancer." HT treatment temperatures range between 40–48°C (104 - 118°F), and the temperature is maintained at a treated site for one hour or more."

"Because of the consequences high temperature may have on tissues, one can refer to use temperatures >50°C (>122°F) as coagulation, 60–90°C (140 - 194°F) as thermal ablation, and >200 °C as charring. Ablation or high-temperature HT is defined as the direct implementation of chemical or thermal therapies to a tumor to reach annihilation or significant tumor destruction."

"The curative capacities, treatment outlay, technical problems, and evidence of efficacy vary depending on the HT approach. While treatment of tumors

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with HT has been applied since the time of the ancient Greeks, this technique has been opposed due to certain limitations. These include:

- failure to heat the target without damaging the nearby cells;
- difficulty achieving homogenous heat dispersion throughout the tumor; and
- inherent problems with targeting invisible micro-metastases."

Heating human tissue with high intensities of microwaves, radio wave, and ultrasound is far from natural. The most natural form of heating is infrared light. Studies on infrared light to induce an artificial fever are few. One study in the International Journal of Hyperthermia does document infrared light treatment.³²⁸ The authors explain,

"Among the different methods of whole-body hyperthermia (WBH), the energy transfer with infrared radiation seems to have established itself as a relatively simple procedure. However, the infrared systems differ concerning the used spectrum of radiation. In the case of water-filtered infrared radiation, infrared A (760 - 1400 nm) is the focal point of heat radiation. This radiation penetrates deep into the skin up to the capillary area of the dermis."

"Eighty treatments of patients in an advanced stage of cancer (40 male, 40 female) were performed with a WBH device with infrared radiation. Extreme WBH was combined with induced hyperglycemia and relative hypoxemia for 83% of the patients with chemotherapy. The body-core temperature was measured rectally or vesically. The objectives of the thermal control were a low rate of side effects and a quick rise of the body-core temperature concerning the condition of the patient's skin. The mean duration of the rising phase (37.5 -41.6°C; 99.5 - 106.9°F) was 87 min."

This study aims to assert the safety of this mode of inducing hyperthermia. In this regard, it was a success. However, no conclusions were drawn regarding the approach's efficacy on the existing cancers. Studies on actual outcomes are sparse and usually involve complementary treatments, not just infrared light-induced hyperthermia.³²⁹

The National Cancer Institute does recognize hyperthermia as a viable treatment. "Hyperthermia is a treatment in which body tissue is heated to as high as 113 °F to help damage and kill cancer cells with little or no harm to normal tissue. Hyperthermia to treat cancer is also called thermal therapy, thermal ablation, or thermotherapy." Infrared light as a facilitator of hyperthermia is not explicitly listed. However, they refer to "placing the entire body in a heated chamber or hot water bath or wrapping with heated blankets." Heating is an inferior way to increase core temperature compared to intense infrared treatment because heating involves conduction. In contrast, infrared light heats as deeply into tissue as it can penetrate.

Infrared Light Hyperthermia Conclusion

Infrared light is the best way to apply hyperthermia, systemically or locally. It is enhanced in combination with red light treatment,

Infrared and red light provides:

- Antioxidants to ensure electrons (energy) are provided to the KREBS cycle (healing);
- Elevated temperatures speed up reactions - of both destruction and repair;
- Elevation in temperature stimulates the production of immunity (cytokines);
- High temperatures are hostile to most pathogens;
- Our tissues have repair mechanisms for any damage created by the natural heating of infrared light, while pathogens may not have such means.

"Go out into the light and warmth of the glorious sun, you pale and sickly ones, and share with vegetation its life-giving, health-healing power."

- The Health Reformer, May 1, 1871

Why Electricity (Electrons) is Fundamental to Health

Your body is a chemical manufacturing and chemical treatment plant. These processes involve combining atoms into new molecules or breaking them down into building blocks or processable waste. Wastes, for example, are sometimes converted to substances more easily handled by the body. These new substances are metabolites.

A computer uses combinations of "0" and "1" to carry out all processing. Your body is similar in that it uses electron donors or electron acceptors.

- Oxidation is when a substance loses an electron (electron donor)
- Reduction (anti-oxidation) is when a substance gains an electron (electron acceptor)

In many instances, instead of a substance gaining or losing an electron, the two components (atoms) share one or more electrons. This occurs when new chemical or biological substances are synthesized, with DNA being an example. It is the assembly of amino acids where each atom when bonded to another, shares electrons.

Redox Reactions: Redox is a common term in chemistry and biology. In chemistry, a redox reaction is one of the chemical reactions involving the transfer of electrons between atoms and molecules. In this reaction, one species loses electrons while the other gains electron. The species that gain the electron is said

to be reduced, while the species that lost the electron is oxidized.³³⁰ Redox is foundational to biological processes such as cellular respiration and photosynthesis. For example, a redox reaction occurs in cellular respiration when glucose is oxidized to carbon dioxide, whereas oxygen is reduced to water. This is similar to burning gasoline in your vehicle engine but is much more efficient because the energy is converted mostly to work, not heat, with the help of enzymes.

In physiology, redox reactions create electron donors and electronic acceptors. In general, electron donors drive repair and recovery reactions. In contrast, electron acceptors are immune molecules that oxidize pathogens. Oxidation kills pathogens by destroying membrane tissue (necrosis). Importantly, to work, the "oxidizing" immune cell must have sufficient oxidizing potential to work. Otherwise, the pathogen will not be destroyed. This explains why some treatments are effective while others are not. Figure 8.11 shows how redox reactions work.

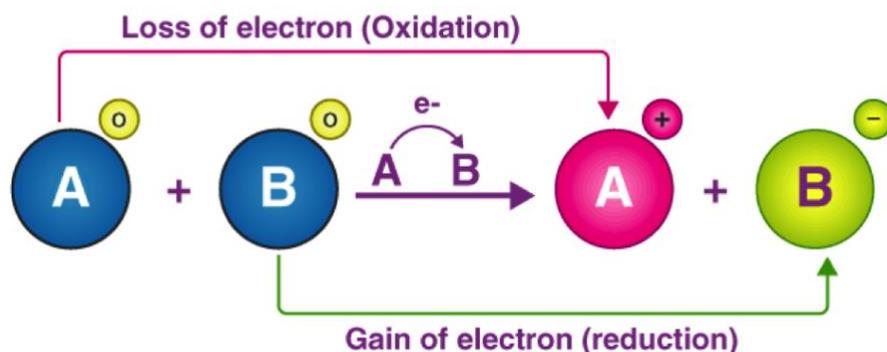


Figure 8.11. Redox reaction.

Consider "A" above to be a pathogen of some type and "B" above an immune cell or an antiseptic like iodine. The pathogen is literally being "burned" by the "oxidizing agent." Oxidized "A" is not viable. Examples of oxidizing agents: are neutrophils, antibodies, peroxides, reactive oxygen species, oxygen, ozone, and iodine.

Electron donors include sunlight, electricity, and food nutrients (antioxidants).

Our bodies can manufacture antioxidants even from an oxidized substance. For example, you do not need to consume iodine in its "oxidized" (anti-infective) form. Potassium iodide is the most common source of the iodine atom. However, the body will expend energy using a peroxidase enzyme and convert the iodide to

iodine. Our body will produce the oxidized form, when needed, to oxidize (kill) a pathogen, for example.¹¹

Another purpose of redox reactions in the living body is cellular communication. Metabolism alters redox reactants both rapidly and transiently, as well as in various long-term steady-states.³³¹ Redox reactants comprise an energy-sensitive communication system within each cell and within cellular compartments. Variations in a metabolic state impact the response of tissues to other communication network systems.

At the most fundamental level, redox creates the flow of electrons. This flow process often creates an electric current, also referred to as electricity. In fact, every cell in our body is a tiny battery, and the charge and magnetic field that results from the flow of current are crucial to the health of all cells.

Electricity: Electricity can be defined as the movement or current of small charged particles, usually electrons. Some substances, such as metals and various liquids, allow the movement of (or conduct) charged particles better than others. The harnessing of electricity has enabled us to develop devices that cause electrical energy to be changed into some other form of energy - e.g., heat (cooking), light (electric bulbs), and motion (electric motors).

The human body, the cells, the organs like the heart and brain, and especially the nervous system are electrical systems. Other systems like the circulatory and lymphatic systems are there to support the health of the electrical system.

The nervous system comprises two parts: the central nervous system, the control center comprising the brain and the spinal cord, and the peripheral nervous system, which consists of nerves connecting other body parts to the control center. This is similar to your home, where you have an electrical hub, the circuit breaker panel, and the internal wiring system supplying electrical energy throughout your home. Organs and tissue are like appliances that convert electrical energy into work. In the body, that work is largely redox (chemical reactions) and signaling. Via a combination of electrical and chemical processes, the nervous system controls the functioning of the entire human body.

The basic building block of the nervous system is the nerve cell, called a neuron. The brain itself consists primarily of neurons. Under a microscope, a neuron looks like an octopus with many tentacles. A neuron can transmit an electrical impulse

11 Some functional doctors indicate they provide a special form of iodine called nascent iodine. This does NOT exist except transiently. Iodine is a diatomic molecule with a dark purple color. Any iodine that is colorless is most likely the iodide salt. You need not worry about the form you take in. If your body needs iodine and you only have iodide, it has the capacity to synthesize what it needs. Functional doctors need to be careful about spreading misinformation if that discipline want to gain credibility

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to the next neuron. The network of electrical impulses enables our body to receive information from the physical world and then send it to our brains, responding by sending appropriate signals through the body. Without healthy neuron circuits, our bodies would completely shut down, like turning off the power supply to a home. That is why the most important aspect of health is supporting our internal infrastructure that supports the health of neurons. In this case, food is thy medicine to ensure your electrical systems are well maintained.

Neurons are similar to computer chips, whereby connections are turned either on or off to send the right signal. Under normal body conditions, the frequency of [electrical pulse] transmission may range between 10 and 500 impulses per second.³³² The impulse is not generated unless the neuron has been given a strong enough stimulus. There may be from ten trillion to one hundred trillion synapses (connections between neurons) in the brain. Each one operates as a tiny calculator that tallies signals arriving as electrical pulses.³³³

Our body commits approximately 30% of its energy to "active transport." This process turns a cell into a battery and produces what is referred to as "charge separation." This means there will be an electric potential across the membrane so that the inside and outside are like a battery's positive and negative poles. Maintaining adequate electric potential in a cell is critical for cellular health and cell-to-cell communication. Certain physiological conditions can disturb this process and cause cellular batteries to be discharged, lacking adequate energy. Eating foods that are low in nutrient content, lack complete digestion or absorption, and infections are usual suspects that disrupt the integrity of the cellular electrical system.

Conclusion

Energy medicine is derived from light, and light is electromagnetic energy. Electromagnetic energy or radiation includes visible light, radio waves, gamma rays, and X-rays, in which electric and magnetic fields vary simultaneously. In electromagnetic medicine, substances are turned off or on to perform a specific repair task or start a cascade of signaling to affect the repair ultimately. Of course, electromagnetic energy may also cause harm through the same process. However, we are exposed to electromagnetic energy daily from the earth, moon, and sun, to name a few sources. We have adapted to mitigate harm from this energy. The proof is that we are alive and energy medicine often helps us thrive. Natural sunlight is healing. The energy from the sun is in perfect balance with us since we evolved and adapted to accommodate the benefits of sunlight and darkness while mitigating harm.

What is the best way to obtain an energy medicine treatment? You want some proven method that is safe, effective, and inexpensive. You also want to work with a practitioner who is competent and experienced. The solution that meets all these criteria is to go outside and get PLENTY of sunshine. You will interact with the entire solar spectrum of light, another word for energy.

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We cannot and will not be the future. Therefore, yield to the next generation with grace. However, our fate is NOT to be sickly and die young. Moses lived 120 years. Most of us will not live that long, but we have an opportunity to live healthy and productive lives.

The age of Moses upon his death is given as 120, at which age "his eye had not dimmed, and his vigor had not diminished."

- Deuteronomy 34:7

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