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A Layman's Guide to Malignancies: Cancer and Cancer Research in Everyday Terms

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A LAYMAN'S GUIDE TO MALIGNANCIES:

CANCER AND CANCER RESEARCH IN EVERYDAY TERMS

by

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ABSTRACT

In the 200,000 years that humans have existed in our current homo sapien sapien form, we built our civilizations based in part on our desire to understand the world around us. The difficult part about this is the fact that our world has grown so vast and so quickly (think Moore's Law, the observation that the speed and capability of computers is projected to double each year with an increasing number of transistors that can fit into a microchip), especially within the past century, that many people have been left behind due to their capability to understand. This gap in understanding is extremely problematic when it comes to issues of importance, such as politics and business. For example, a significant portion of the population does not understand the electoral college and its role in ensuring that the few do not decide for the many in our Presidential elections. On a more personal note, healthcare is unnecessarily complex, from advancements in treatment, the structure of insurance, how care itself is delivered, and how "health" is perceived. While one guide cannot cover all of the intricacies of the medical field, this thesis discusses a complex disease that affects millions of patients and their families each year. Cancer biology, treatment, and research will be explained using science, history, and mathematics in layman's terms.

TABLE OF CONTENTS

INTRODUCTION

Of the prevalent yet misunderstood human afflictions, cancer is perhaps the most prevalent and most misunderstood of them all. Basic cancer rates are relatively straightforward to quantize. In a 2015 study, the Centers for Disease Control and Prevention (the CDC) determined that cancer is the second leading cause of death in the United States, surpassed only by heart disease [1]. In total, one in four deaths in the United States is due to cancer.

Cancer rates (from the same 2015 study), both by new cases reported and by death, were determined per 100,000 people for each state. The national average for diagnosis was 438 and 159 for death. The State of Maine was one of four states that exceeded both of those averages with a new case rate of 468 (ranked 11th of 50 states) and a death rate of 177.5 (ranked 13th). There are many factors that may contribute to these sobering statistics, including the State's aging population, rural landscape (which makes access to adequate medical care difficult for some), sedentary lifestyle, low screening rates, the prevalence of granite, the poor air quality from Maine being "the tailpipe of the nation," and the state's poverty rate [2,3].

Risk factors such as these are apparent in all walks of life. Seemingly perfectly healthy people will be struck down by a disease that can manifest itself due to genetics, age, lifestyle, and even the environment. Ordinary people are often unprepared for the world of sickness, treatment, and remission. The average cancer patient may feel as though they have no power over this disease or their body. Everyone deserves to know exactly how their body works, how it might be malfunctioning, and what the possible treatment options are because individuals should have autonomous control over their body, which is the only possession that truly belongs to them. Individuals always have choices as to how they interact with their disease, and this can be the difference between a successful or an unsuccessful treatment regime. Knowledge can empower these individuals to advocate for themselves and make more effective decisions. Lack of understanding is dangerous because it can (and has) led to people giving the power to make important decisions to others, who may or may not have their best interests in mind.

At age nine, I watched an uncle and an aunt battle cancer unsuccessfully. Another uncle became sick a few years later and did not seek treatment. I had a basic understanding, from a very young age, about cancer and cancer treatment. My aunt explained to me why a stem cell transplant was necessary to treat her multiple myeloma and why she could not buy bread from the supermarket bakery in a way that made it seem like she had everything figured out. Whether or not understanding her treatment actually helped her, my aunt's understanding most certainly helped my family cope when we realized that she was not going to get better. At age nine, I was not asking my aunt if being educated about her disease and treatment helped her to fight or at least cope. However, my personal understanding of the mechanisms behind the echocardiogram tests that followed reparative surgery for my heart murmur greatly helped my preteen self during check-ups.

My relatives were generally educated about their disease, however many others are not. A 2008 study using data from the National Cancer Institute (the United States' federal government leading agency for cancer research) found that when surveyed, less than half (44.9%) of Americans had ever searched for cancer information. Additionally, and according to the same source, “Many [people] reported negative experiences, including the search process requiring a lot of effort (47.7%), expressing frustration (41.3%), and concerns about the quality of the information found (57.7%) [4].”

It may seem like the greatest injustice to be thrust, generally weaponless, into the fight against cancer as a cancer patient, but this thesis is an attempt to arm the average person in this complex fight. Having a greater understanding of these things (medicine, business, law, technology) that make our existence complex offers improvement in the quality of life. Truly living requires more than simply going through the motions. Being better educated allows people to experience their own lives. In medicine, instead of experiencing cancer a vast unknown that requires professional interference and incomprehensible medicine, a person can approach it as a disease to be healed.

A person should know what the difference is between a healthy cell and a cancer cell, understand the nature of cancer, know the risk factors, the treatment methods, and all of the ways in which cancer statistics, from research spending to screening statistics, can be extremely misleading. Knowledge is a powerful tool. It can change everything from your mindset to the type of treatment you receive to the outcome of your diagnosis. This thesis is one snapshot of the science, history, and mathematics of cancer for the everyday person.

PART I: THE CELLS THAT WORK TOO WELL

According to the American Cancer Society, a nationwide voluntary health organization established in 1913, a person has a one in three chance of developing cancer as of 2019 [5]. The vast majority of people will know someone, or many someones, who have been afflicted with cancer. In a group of three people, that someone who develops cancer may very well be you. While cancer is relatively common, knowledge about it is not. Cancer is an umbrella term that encompasses over a hundred distinct diseases, and that can be overwhelming. Cancer is a disease that is commonly feared because it is not understood due to that complexity. Despite (or perhaps due to) the justifiable fear, the statistic that one third of the world's population has the chance of developing cancer shows just how imperative it is that everyone understand this disease because it does not discriminate. The very first step in this understanding is knowing how the most basic unit of life, the cell, functions when it is healthy and when it becomes cancerous.

CHAPTER I

THE STUDY OF HEALTH

Modern medicine, and especially the medicine that characterizes Western civilizations such as the United States, can be classified as curative. This means that our current practices concerning our health are focused more on treating the disease, not the cause. We have a terrible habit of going through life without considering the consequences of science and taking for granted that everything works out as it is supposed to. The only time that we take a moment to reflect on how the world works is when curiosity peaks our interest, and that most often happens when we observe that it stops working as we expect it to.

To understand cancer, we must first have a grasp on science, and more specifically, on biology and how our bodies work when they are healthy. After all, cancer is a disease of the cell. Biology, the most tangible natural science, is often classified as the study of life [6]. Biology becomes its own discipline in science on the cellular level, because despite its leaning heavily on physics and chemistry to explain its phenomena, it is the cell that is the building block for all living things.

Humans, and other complex animals, are composed of trillions of cells. Our cells are extremely varied in both shape and function, which is evident in the of study anatomy and physiology. Cells range from gigantic and branching (neurons) to simple water-filled sacs (red blood cells), and absolutely everything in between. Our cells are the basis for understanding how we function and included in that is the pathway to linking cancer as a disease to humans. Cellular biology is a vast and fascinating field. Studying the most fundamental unit of what makes us living beings is extremely significant in understanding what we are and how we function [7]. Cells are more than a cycle of reproducing and dying, they are key to our living.

For complex living things, cells compose tissues. Tissues, sometimes many different types of tissues, compose organs. Within our bodies many organs compose organ systems that allow us to operate the way that we do. Organs systems (nervous, cardiac, skeletal, pulmonary) come together to compose organisms such as ourselves. It is this hierarchy that allows a disease of the cells to become fatal to the entire organism.

On the other end of the spectrum, cells are small units of life capable of a life cycle or growing, reproducing, and dying that is not overtly different from organisms such as ourselves. They have organelles not unlike our organs that perform specialized functions within the cell. Those organelles are composed of macromolecules which are formed from different elements which are collections of atoms, which make up all of matter, at their base.

When considering cancer, the most important organelle in the cell is the nucleus, which is the main brain behind cell function. The nucleus is the overall control center of the cell, capable of sending directions for the cell to grow, divide, or die. In human cells, the nucleus is a membrane bound organelle that contains the genetic material of the cell, deoxyribonucleic acid (DNA), in multiple, linear molecules that are coiled into structures called chromosomes.

DNA contains instructions necessary for the development, survival, and reproduction of an organism. These functions are transcribed into messages via ribonucleic acid (RNA) and then those messages are translated to produce proteins, which are complex molecules that enable the physical work in our bodies. Each DNA sequence that becomes the instructions a function (sometimes these are proteins) is called a gene. Genes are only about one percent of the DNA sequence, or genome. The rest of the sequence is responsible for regulating the production of proteins as the cell requires.

Normal, healthy cells will grow and divide as the body needs them to, and they do this in a process called the cell cycle. The cell cycle is the process by which a cell makes a copy of its DNA and then divides into two daughter cells. An important trait of the healthy cell is that it only functions while it is able to do its preprogrammed job. When cells get damaged or simply grow old, they die in a process called apoptosis (programmed cell death), which allows new cells to take their place.

Understanding the cell cycle is key to understanding how cancer develops and how it can be treated. Many cancer-fighting medicines work by interfering with the cell cycle. To start, there are four stages of the cell cycle: G1, G2, M, and S. The “G” in G1 and G2 stand for “gaps,” and during these stages, which occur in between the M and the S phases, nothing appears to be happening in the nucleus of the cell although the cell itself is very active and preparing to grow and divide. “S” stands for synthesis, which is the point in the cell cycle where DNA is replicated, and “M” stands for mitosis, which is the actual cell division. The two stages that are especially important in the conversation about cancer are synthesis and mitosis.

DNA replication, or synthesis of the cell cycle, is the process by which each chromosome in the cell is copied. This requires a large number of enzymes, which are protein molecules that aid in biochemical reactions, such as those required to copy DNA. In DNA replication, each double-stranded DNA is unwound and the separate sides are used as a template for a complementary strand. The end result is two identical copies of the genetic material.

Mitosis is the phase of the cell cycle where a single cell divides into two daughter cells with identical genetic content of the parent cell. Cancer cells, however, do not always have the same genetic content as their parent cell. Mitosis occurs in four steps: prophase, metaphase, anaphase, and telophase. In prophase, the nuclear envelope that isolates the nucleus of the cell dissolves, chromosomes condense, and spindle fibers (protein fibers that provide structure for the dividing cell to move cell components and form the two new cells) form. In metaphase, the replicated chromosomes line up in the middle of the cell in preparation for division. Anaphase is where the chromosomes become elongated and form distinct poles, and during telophase, two nuclear envelopes form and new cell membranes are formed to create two cells.

The time in which a cell is between cell divisions, and the phase that cells are in most of the time, is called interphase, where the cell is simply performing its function in the body. All of the above describes the normal, healthy cell. Cancer disrupts the normalcy and causes cells to grow out of control. The next chapter will describe how the cancerous cell develops and is different from the healthy cell. In context, cancer generally develops from mistakes in synthesis, and cancer treatment typically targets cells during mitosis.

CHAPTER II

THE SUPERPOWERED CELLS

Cancer is the name of not one, but many different diseases of the cell. In general it describes the phenomena of uncontrolled cell growth, where some cells, instead of following the orderly process of the cell cycle, begin to divide without stopping and spread to surrounding tissues.

Despite cancer's ability to manifest itself in over one hundred different diseases, all of them stem from one root cause: changes to the way that our cells grow and divide that result from changes to the genes that control the ways in which our cells function. In sum, cancer is a genetic disease. As discussed previously, genes are specific sequences of DNA that code for a function. Genetic changes can be inherited from our parents or they appear during our lifetimes from errors that occur during cell division or from DNA damage caused by certain environmental factors. Errors during cell division are actually quite common, however there are many enzymes within the cell that work to fix these mistakes. The environmental factors that cause DNA damage are relatively well known, and include the smoke from cigarettes and excess exposure to UV radiation from the sun.

Any change in the DNA sequence of a cell is called a mutation. A mutation does not necessarily lead to cancer or a serious disease, some can actually be beneficial (e.g., virus immunity) or have no effect (e.g., result in different eye colors). The gene changes that cause cancer are specific mutations that might increase the production of a protein that causes cells to grow or they might produce a misshapen protein that does not function normally, which would be especially detrimental if that protein's function is to repair cell damage. Cells with these genetic mutations have a tendency to develop additional mutations in other genes, and these compounded mutations can cause cells to become cancerous, where they grow without stopping and spread throughout the body.

The cells in our bodies are meant to grow and divide to help us grow and function normally. However, cancer causes our cells to grow and divide to a greater extent than our bodies need, and in a sense, they are working *too* well [8]. The main consequence of cancerous cells is that they do not function as they are supposed to and they have the capability to crowd out normal cells and interrupt the function that they are meant to perform [9]. Take, for example, leukemia, which is cancer of the bone marrow where blood cells are formed. Blood cells, and in particular red blood cells, are responsible for transporting oxygen and nutrients to tissues all over the body and carbon dioxide and waste materials away from these tissues. Leukemia causes a build up of abnormal white blood cells, which normally help to fight infections, in the blood and bone marrow and effectively crowd out red blood cells so it is much harder for the body to deliver oxygen to its tissues, control bleeding, and fight infections.

Any organ in the body is capable of developing cancer. This is because every organ is made up of tissues which are made up of cells, and each and every cell has DNA that codes for genes that have the capacity to undergo changes. There are many different kinds of cancer because the human body requires many different kinds of cells that perform the complex functions to keep us alive. Because our cells are so different, cancers of different types of cells are evidently different. Some types of cancer, such as melanoma, skin cancer, are very common and have entire populations of people that are more susceptible. Other cancers are rare, such as thyroid cancer, where less than two in

10,000 people are diagnosed each year. Some cancers spread quickly (lung cancer), and others take decades to develop, (non-Hodgkin's lymphoma). Some, such as breast cancer, often result in tumors, or masses of cell growth (though a tumor is not always cancerous, some are benign), and others will not, as with blood cancer. Cancer is often named after the organ in which it originates, however there are many cancers subtypes that are distinguishable from which cells are affected or by the rate at which the cancer may spread. This explains the four common types of leukemia.

Cancer varies by type as to its mortality rate. Some cancers are detected too late for any kind of effective treatment. This is often the case with pancreatic cancer, which is typically diagnosed as Stage IV cancer. A common trait of cancer is its tendency to spread to surrounding tissues, and this is termed metastasis. Metastasis occurs through the circulatory system or the lymphatic system and form metastatic tumors. The amount that the cancer has spread often corresponds to the seriousness of the disease. Prognosis is often measured in stages, numbered I through IV [10]. Stage I breast cancer means that the cancer is evident but still contained to its area of origin. Stage IV breast cancer means that cancer has spread to other parts of the body and successful treatment is more difficult. Other cancers are more deadly due to the nature of the cancerous cells. Glioblastoma, a form of brain cancer, is notoriously difficult to treat because its normal cells are star-shaped and develop tentacles when they become cancerous. These tumors are very difficult to remove via surgery and advance rapidly because they can control surrounding blood vessels that feed cancerous cells.

In sum, cancer is a very complex disease. How it develops and the multitude of different disease types is a direct result of our complex cellular biology. These variations also result in many different treatment procedures and risk factors, which will be discussed next.

PART II: AN UNNATURAL HISTORY & THE "RACE" TO CURE

As long as cancer has been distinguishable from other diseases, people have been looking for cures [11]. Cancer research has been divided into two distinct branches: (i) a race to find a way to cure the typical cancer patient and, (ii) work to understand how cancer develops in the first place. Notable progress on the former started in the 1940s with Dr. Sidney Farber (after whom the Dana-Farber Cancer Institute was named) and his work to combat pediatric acute lymphoblastic leukemia [8,12]. This disease is a very rare form of blood cancer, and he turned to "antifolates," which are synthetic chemicals that inhibit DNA replication. These efforts earned him the title of the father of modern "chemotherapy." Almost fifty years before Dr. Farber started his first trials at Boston Children's Hospital, Dr. William Halstead was performing radical surgery in an attempt to cure breast cancer and Dr. Emil Herman Grubbe was using radiation as a means to shrink tumors [13,14]. Today, these three treatment methods (chemotherapy, surgery, and radiation) have become much more precise and effective through many years of trial and error. Additional studies of cancer have brought to light common risk factors and possible new treatment methods such as immunotherapy and the controversial CRISPR technology. Cancer has followed a unique path through history. Even before scientists fully understood DNA, they were using X-rays to damage it in an attempt to cure cancer. Unlike a normal progression of events, cancer started large, with tumors and explosions of white blood cells, and has become small, with the discovery of its root cause (DNA damage). Somewhere in the middle, scientists and medical professionals were able to determine the factors that cause cancer, and that all sums to an unusual series of events.

CHAPTER III

TREATMENT

Scientists and physicians have been developing treatments for cancer long before we understood how it arises from a genetic disease. There are many variations of cancer treatment because of the variety of the disease itself, but also because of the differences between patients. The three main types of cancer treatment that have dominated the field in the past century and are still used today are chemotherapy, surgery, and radiation. Medical advancements and increased knowledge on what causes cancer have resulted in even more treatment types, which will be discussed in the next two chapters.

The cancer treatment that has a great deal of visibility, especially in the treatment of metastatic cancer, started ironically, as a poison. Chemotherapy (chemo) is the use of any medicine or any drug to treat any disease. In general, chemotherapy is a type of cancer treatment where anticancer drugs can be administered orally, through pills, or intravenously.

During World War I, chemical warfare was introduced as a formidable weapon. Mustard gas, one of many chemical agents used at the time, was found to be effective in ceasing cell division, and provided the potential for a means of suppressing the cell division of cancerous cells. Thankfully, World War II did not see further use of chemical warfare on the battlefield, but it did see a new approach to cancer therapy pioneered by Dr. Sidney Farber. His work to use antifolates (anti-folic acid) to treat acute lymphoblastic leukemia was the beginning of modern chemotherapy. In fact, a drug that Dr. Farber worked with in the 1940s, methotrexate, is still used today.

Chemotherapy generally describes the treatment process whereby a selected drug or drugs, the order of their use, their dosages, and chronology of their use depend on the cancer (type, stage) and the patient (age, health, medical history). The intended use of chemotherapy is also considered, since the chemotherapy may be used in an effort to cure, to control, or simply to lessen the symptoms of the cancer.

Anti-cancer drugs themselves work to target different stages of the cell cycle, thereby hindering the formation of new cells. Some specific anticancer drugs include alkylating agents (cause damage to a cell's DNA, hinder reproduction), antimetabolites (interfere with DNA growth), anti-tumor antibiotics (changes the DNA of cells to keep them from growing and multiplying), topoisomerase inhibitors (interfere with enzymes called topoisomerases which aid in the process of copying DNA), mitotic inhibitors (stop cells from dividing), and corticosteroids (used to prevent nausea, vomiting, and severe allergic reactions).

As chemotherapy drugs cannot always tell the distinguish between healthy cells and cancer cells (which do have a tendency to grow more quickly than normal cells), chemotherapy often causes damage to both. Unintended damage to healthy cells can cause many different side effects. Perhaps the most well known side effect of chemotherapy is hair loss, however the cells of the mouth, digestive tract, and reproductive system are commonly damaged by chemotherapy. In some cases, the side effect is more cancer as the cells in bone marrow are also at risk for damage, which can lead to leukemia.

Not everyone undergoing chemotherapy experiences side effects, and every experience is different. There is a delicate balance between the chemotherapy drugs being powerful enough to treat cancer but not so powerful that they cause serious side effects. Combinations of different anticancer drugs are often used to make treatment as effective as possible. Today, ongoing clinical trials are constantly making efforts to develop new drugs or better treatment plans (varying doses, orders, etc). Treatment today is significantly more effective and causes fewer side effects than it was one or more decades ago.

Chemotherapy, which began as a cure for blood cancer, is especially useful to treat cancer that has spread throughout the body. Other therapies (radiation, surgery) are used to treat localized cancer.

Surgery as a means of cancer treatment existed long before chemotherapy. At first, it was used only as a means to treat cancer. The best example of this is the radical mastectomy, which was a common treatment for breast cancer in the early to mid 1900s. William Halstead published a paper in 1894 documenting fifty cases of surgical therapy for breast cancer at Johns Hopkins Hospital. This procedure prevailed for over seventy years, and prompted the removal of all breast tissue, the surrounding skin, axillary lymph nodes, and muscles of the chest wall, including the pectoralis major, rectus abdominis, serratus anterior, subscapularis, latissimus dorsi, and the teres major muscle. While Halstead achieved an unparalleled survival rate, the patients who endured a radical mastectomy suffered from increased mortality rates from large, post operation wounds. Quality of life for these patients was severely decreased. With a compromised lymphatic system, women suffered from lymphedema. Removing the chest muscles restricted arm movement and resulted in chronic pain in addition to the radical disfigurement. Later studies would reveal that radical mastectomies did not improve the chances of patient survival if the cancer was in a later stage.

Starting in the mid 1900s, cancer surgery has become much less invasive. Surgery is perhaps the most evolved form of cancer treatment and serves a significant percentage of cancer patients (especially breast cancer). In modern medicine, this method of cancer treatment is generally used to remove the physical manifestations of cancer, such as tumors. However, it is also used to prevent, diagnose, stage, and treat cancer. A physician can take a tissue sample of a lump or a growth and analyze it for cancerous cells (a biopsy). He or she can fully remove a growth or lump as a preventative measure or as treatment. Physicians can also use surgery to observe surrounding organs and lymph nodes to see if the cancer has spread, which is called staging. In some cases, surgery is only a means of relieving the symptoms of cancer if full removal is not possible or would damage other organs. Cancer surgery has also evolved to reduce risks associated with any surgery. New techniques including using lasers, cryogenics, electrical currents, radiofrequency, and other methods are meant to reduce the invasive nature and improve the effectiveness of surgery.

Two years after Dr. Halstead presented the results of his radical mastectomy trials, German physics professor Wilhelm Conrad Röntgen presented on his discovery of X-rays. X-rays refer to a specific, high energy wavelength range of electromagnetic radiation. Even before understanding the physical properties of X-rays and their effects on human biology, new techniques involving X-rays were being developed for cancer treatment. First, what we know as radiation therapy, or radiotherapy, involved using X-rays as a way to image and detect possible tumors. These techniques evolved to include other types of radiation (gamma rays, electron beams, or protons) and to treat cancer with advances in radiation physics and computer technology. This type of treatment uses high-energy waves projected onto cancer cells to make small breaks in the DNA within the cells. This effectively stops the cells from growing and dividing, and then the cells will die. Radiation can also affect nearby healthy cells, but most will recover and resume their original functions.

At the beginning of the twentieth century, breast cancer and skin cancer were treated using radiation. With the ability to create high energy X-rays to treat deeper cancers, radiation was discovered to have the capability to both treat and to cause cancer. In early trials, before there were systems to focus the radiation onto local tumors and before dosing was determined, the benefits from cancer treatment were not balanced by the side effects they caused. Even today, the most common side effects are fatigue and hair loss and skin changes in the specific targeted area of treatment.

Radiation therapy as cancer treatment is very common. There are two main types of radiation therapy which are essentially external beam or internal. The type of treatment depends on your specific cancer, such as tumor location and other planned treatment. External beam radiotherapy is given by a specialized machine capable of aiming radiation to specific target areas such as your chest for lung cancer. Internal radiotherapy is where a source of radiation is put inside your body and this could be in liquid (systemic therapy) or solid (brachytherapy) form.

Radiation is used to treat many different types of cancer, however the treatment itself is only effective for localized cancer. Radiation may be the only treatment that a patient needs, or it might be used with other treatments to improve the effectiveness of those treatments. In some cases, radiotherapy is used for localized cancers where surgery is not possible, such as cancer of the eye.

Developing effective cancer treatment has been a long road of trial and error. Even today, with treatments that surpass historical methods by lightyears, there is room to improve.

CHAPTER IV

FUTURE PRACTICES

The current methods of cancer treatment encompass three broad yet distinct fields of study, which is a significant arena in which to explore cancer treatment. All three have been around for a century or more, at least in theory, and have developed from sometimes disastrous beginnings to be effective treatment methods. Another worthwhile note, and an observable fact in most of modern American medicine, is that all three of these treatments are known as “curative” medicine, in comparison to preventative medicine.

A common critique of curative medicine is that the treatment is for the symptom, which is significantly less effective than treating the cause. As cancer treatment has benefited from the vast amount of knowledge we have gained in the field of cellular biology, both treatments and studies into the causes of cancer are continually improving. This rather illogical progression, from cancer to the cell, which also resembles our trek through chemistry and physics, is nothing new in the process of human discovery. Preventative medicine, on the other hand, is rarely talked about because it is not economic. In the case of cancer, given what we know about genetic mutations, this is probably not in our near future because of the ethical concerns of gene editing. However, the technology exists that could make this a reality. Hopefully by the time this happens, we understand enough about ourselves to use it responsibly. There is a medical middle ground between preventative and curative medicine which encompasses early detection and early action.

An up and coming cancer treatment is immunology, or the branch of biology concerned with the immune system, the organs, cells, and substances within the body that provide protection against infections and some diseases [15]. Any foreign substance, such as a germ, will be recognized by the immune system and “attacked.” The immune system falls short with cancer cells because these are not always different enough from healthy cells for the immune system to recognize them, or the response of the immune system is not strong enough to destroy the cancer cells.

Researchers have developed several ways to aid the immune system in recognizing and destroying cancer cells, including monoclonal antibodies (man-made immune system proteins) that can be designed to attack specific parts of a cancer cell, cancer vaccines which will start an immune response to certain diseases, or immune checkpoint inhibitors, which are a general aid to the immune system. A great advantage of immunology is its use of systems that are already within the body.

A possible future cancer treatment method may employ CRISPR (clustered regularly interspaced short palindromic repeats) technology, a family of DNA sequences found in organisms such as bacteria and archaea that can be reprogrammed to track down and edit genes in any organism [16]. As our genes are the code for everything that makes us who we are, this is an extremely powerful and dangerous tool. CRISPR is not currently being used for cancer treatment. Currently, it is being used in clinical trials to reduce genetic deafness in mice, but the potential, and the excitement, is already there and moving quickly. The human genome was successfully mapped only fifteen years ago and this is a large advancement.

These are the future of cancer treatment, the development of which has only been possible from past trial and error.

CHAPTER V

RISK FACTORS

When Sidney Farber first started developing chemotherapy in 1947, the root cause of cancer was still unknown. Years of research revealed that genetic mutations that cause cancer cells to divide uncontrollably, and these genetic mutations can occur from inherited traits, carcinogens, age, and even lifestyle choices. The average person who has a chance to become a cancer patient (meaning everyone) can utilize the powerful tool of understanding risk factors to lower the odds of developing cancer.

Increasing awareness about the link between health and cancer risk is a critical step for everyone in understanding cancer. One of the best ways to prevent cancer before it has even started is to take care of your body with proper diet, exercise, and lifestyle [9].

Some aspects of a healthy lifestyle reducing cancer risk are not widely known. Even smoking cigarettes (and other tobacco products), which has long been a known cause of lung cancer, was not properly advertised as such on cigarette packs until the 1960s. Physicians and scientists have understood the link between smoking tobacco and cancer since the 1760s, however tobacco companies were not keen to add warning labels with the word “cancer” on them [8]. This is not the only example of industries putting profits before human health. Today, smoking is still the cause of 90% of lung cancer cases in men and 80% of lung cancer cases in women. Lung cancer is the second most common type of lung cancer (after skin cancer) and it is the deadliest of all cancers. Taking protective measures like quitting smoking, not smoking at all, and avoiding secondhand smoke will all drastically reduce lung cancer risk. Avoiding environmental factors such as radiation exposure, knowing your family history for lung cancer, being vaccinated against HIV, and maintaining a healthy lifestyle will also lower your risk of lung cancer.

Many common cancers have similar risk factors that can be easily reduced provided more awareness and understanding. Wearing sun protection and avoiding direct sunlight in the middle of the day is an effective way to lower your risk of many types of skin cancer. Staying active and eating a healthy diet has been linked to lowered risk of breast, colorectal, esophagus, kidney, and pancreas cancers. Additionally, a healthy lifestyle has other health benefits such as lowered risk of heart disease. Certain viruses, including HIV, have been linked to cancer. Vaccinations against the human papillomavirus (HPV) during childhood are expected to prevent 90% of six types of cancer that can result from infections due to the virus. However, not every type of cancer is preventable by simply exercising or eating vegetables.

Some people are at an increased risk for cancer because of inherited genes. For these types of cancer, there are no precautionary methods you can really take besides knowing your family history and the signs and symptoms in order to be screened effectively. Breast cancer, pancreatic cancer, melanoma, and retinoblastoma fall under this category or at least have been known to arise from inherited genes (breast cancer risk can be lowered by maintaining a healthy lifestyle and melanoma risk can be lowered by avoiding UV radiation, see above). One last, inevitable cancer risk factor that follows the same vein as inherited genes is age.

The more common types of cancer are often age-related. Various tests have been developed to screen for these types of cancer, which can detect cancer before a patient has developed any symptoms (which is not always a good thing, as we shall see). The guidelines for undergoing these screenings reflect the impact that age has on cancer risk. After age 40, women should consider getting annual mammograms to screen for breast cancer, and all women should be aware of what their breasts normally look and feel like. At age 45, people of average risk for colorectal cancer should be regularly screened. Women who are 21 and older should have a Pap test regularly to test for cervical cancer. People who are at higher risk for lung cancer, those who are older than age 55 and have a significant smoking history, should get yearly screenings with a low-dose CT. Prostate cancer screening has pros and cons, which men need to be aware of starting at age 50 to decide whether or not to be tested. Women entering menopause should be told about the risks and symptoms of endometrial cancer. In total, over three-quarters of new cancer cases diagnosed are in people age 55 or older.

Aside from risk, another important cancer factor to be familiar with are the symptoms of cancer. Some symptoms are prominent and warrant immediate attention, especially in the case of tumors, swollen lymph nodes, or unexplained, persistent weight loss or fatigue. However, as with the nature of cancer itself, risk and symptoms are highly varied due to the complexity of the disease. The important factor here is recognizing that staying healthy and aware of cancer risk does not have to be overly complicated. These two actions alone dramatically reduces the risk of many different kinds of cancer. We are only aware that we can reduce our cancer risk because cancer research has uncovered the mechanisms of cancer. This approach to a cure has come secondary to finding effective treatment, as discussed in the previous chapter, but more and more focus is going towards treating cancer itself, and not just its aftermath.

PART III: BY THE NUMBERS

As with any science-based field, cancer involves mathematics and statistics. The turning point of Dr. Sidney Farber's research was made possible because leukemia can be counted, or the amount of white blood cells in a sample can be quantized. However, where there are numbers, confusion often follows. In a 2017 study of high school students by the Thomas B. Fordham Institute, an overwhelming 34% of students cited math as their least favorite subject [17]. The runner up in this category was English language arts, however there is quite a difference when only 14% of students state that ELA as their least favorite. Mathematics, in spite of the difficulties, serves the important function of allowing us to see the big picture. Whether or not this is obvious, math is present in many of our daily interactions, from telling time to preparing food. So many life skills require a basic understanding of math and statistics. With cancer, numbers are equally as abundant. Everything from risk put into lifetime odds, money donated to a cancer research cause, and statistics that detail the effectiveness of screening and treatment can become complicated quickly because they are based on numbers.

CHAPTER VI

RESEARCH SPENDING

Cancer research remains a budding field in its two pronged offense as described above. Improving current treatments, developing new methods, and gaining a better understanding of what causes cancer in the first place (and risk factors and methods to lower those risk factors) has taken a significant amount of time but also a significant amount of money.

Cancer research requires funding. Thankfully, human health is seen as an important investment to the federal government and cancer research has significant base ongoing funding. In 2019, $5.74 billion in cancer research was funded by the federal government through the National Cancer Institute (NCI), an affiliate of the National Institutes of Health (NIH) [18,19,20]. Researchers from universities and private research institutes, such as John Hopkins, St. Jude's, Memorial Sloan Kettering Cancer Center, and others, compete for these research funds. Organizations like the American Cancer Society (ACS) and Susan G. Komen Foundation fundraise for research and those funds supplement grant money from the NCI, however non governmental funding is a drop in the bucket compared to the collective federal funds. This does not mean that privately funded institutions are not worth donating to, because both ACS and Susan G. Komen are more than just an intermediary for research. They both provide significant resources for those that need information or patients that require financial support.

However, people should be fully informed about the non-profit organizations they chose to donate to [18]. Controversy in the early 2010s surrounding Susan G. Komen began with their fundraising partnerships, CEO's salary, and connections with companies that benefit from more breast cancer patients. Susan G. Komen, as of 2017, is reportedly donating about 40% of funds raised to cancer research, which is an improvement from only 21% in 2010, but still falls flat as an organization that has claimed to be "for the cure" [22]. In 1982, when Susan G. Komen was founded by Nancy Brinker, this organization was instrumental in spreading awareness of breast cancer, a disease previously viewed as too "taboo" for published newspapers [8]. It is up to an individual to decide if an organization's mission and actions line up with their personal beliefs.

Non-profit organizations do donate to research efforts, the amount, however, may come as a shock to some. Every company requires overhead. They need to keep their lights on and pay their employees. However, there is an amount that is reasonable, and an amount that might indicate your donation will be more effective elsewhere. While the NCI does provide lots of funding, money available for research grants is highly sought after and can be very restrictive. Perhaps a scientist working in a university lab has a creative idea on a new method of cancer treatment. They might benefit from discretionary funds, which can be delivered through the NCI or other charities, that would allow them to collect preliminary data and gain federal funding.

As non-profit cancer organizations commonly subsist from public donations, those donors have a right to know where their funds are being channeled. If you do not agree with what annual reports are telling you, feel free to choose another organizations or cause. Something that few people think about when they donate to the cause is the fact that cancer research and drug development research in general is an extremely slow process. Years of clinical trials are required to put a new treatment on the market. If you want to see your donation make an immediate effect, research probably is not a good choice. One of the best and overlooked ways that individuals can give to the cancer fighting effort is to contribute to charities that work to improve the quality of life for cancer patients.

The fact that something as simple as donating money to help fight cancer can become so confusing so quickly, but understanding is very possible and very empowering. People just need to know what they should be looking at.

CHAPTER VII

CANCER STATISTICS

If cancer funding turned out to be more complex than expected, cancer statistics are a completely different struggle. Perhaps the most difficult aspect of cancer research is the need to prove that work being done is effective. This sounds counterintuitive, but true because the nature of reported cancer statistics are more complex than numbers that can be easily reported.

For example, women have a one in nine chance of developing breast cancer during their lifetime, which is highest odds of any type of cancer. The fact that people generally fail to recognize this is the fact that cancer, along with being related to health and living environment, is also an age-related disease. At age 40, a woman’s odds of developing breast cancer are actually only one in 400. Risk grows exponentially with age, however general statistics do not reflect that. The odds of developing cancer, for both males and females, is one in three (cancer has decreased in males recently, the odds were previously one in two) and the odds of dying from cancer are one in five, but that is over an entire lifetime.

Of course, this is simply overall cancer risk. The complicated portion comes from measuring the effectiveness of cancer screening statistics as well as cancer treatment effectiveness.

To start, clinical trials have shown that routine screening for breast cancer, and other common cancer types such as cervical, colorectal, and lung cancer, does save lives. However, thanks to the evolving understanding of cancer screenings, recent trends have shown that less screening is recommended. For breast cancer in women aged 50 to 59 in particular, 1,300 women need to be screened to save one life. There are even studies that show the excess screening can lead to false diagnosis and unnecessary anxiety. The confusion comes from the use of survival, the measurement of how long a person lives after diagnosis, to judge how effective cancer screening is at saving lives.

Survival is not an accurate measure of screening effectiveness due to two types of bias: lead-time and length [23]. Lead-time bias is when cancer screening finds the cancer earlier than the cancer symptoms would have revealed said cancer, but the earlier diagnosis does not change the course of the disease. This is best explained by the following example: "A man experiencing a persistent cough and weight loss is diagnosed with lung cancer at age 67, and he dies of his cancer at age 70. The five-year survival rate for this man, and others like him, is 0%. If this same man had been screened and his cancer detected earlier, perhaps at age 60, but he still dies at age 70, his life has not been extended, but the five-year survival rate is 100%." This seemingly increased survival rate is inaccurate and completely misleading about the nature of cancer screenings.

Length bias, on the other hand, skews numbers and contributes to overdiagnosis. This is especially the case with slow-growing, less aggressive cancers, which will never cause harm or require treatment for the entirety of the patient's lifetime. However, if screened, treatment will proceed and create another disproportionate five-year survival rate. The hypothetical example is that there are 1000 people with a form of progressive cancer. After five years, 400 are alive and 600 are dead. This means that the survival rate is 40%. When 2000 other patients are over diagnosed because their cancer is nonprogressive, but the same 1000 people have a progressive cancer, the same number of people have died, but the survival rate appears to be 80%, an alarming discrepancy.

The odds of a person developing cancer, cancer screening, and treatment statistics can be misleading. Cancer is more than one mathematical expression that describes the risk for a person to develop any disease that was caused by uncontrolled cell growth at any time during their life. These numbers should be much more specific to age and cancer type, but one thing that is extremely effective is the fact that the advancements that brought this confusion also brought a greater understanding of the disease itself. The average person does not understand how cancer really and truly works, but, with a little help, they can.

CONCLUSION

Cancer, from its nature to its history to its numbers, is an undeniably complex disease. Despite the fact that this is a disease that has the capability to affect up to one third of the population, few understand how it works from start to finish. Even with the discussions started here, there is even more that contributes to the industry of cancer. This is merely one peak of the mountain of information a person must submit to fully understand medicine, but it is an excellent starting point.

The truth of cancer is darker than most people can imagine. This disease has inspired as massive, extremely lucrative industry that includes billion dollar non-profit organizations, companies that manufacture screening equipment, and the ever present "big pharma" still plugging away at that miracle drug that will save us all. When cancer patients are kept in the dark about the nature of their disease and their treatments, they are the ones that pay much more than money for a corporation's greed.

Despite that, all hope is not lost.

The start is education. This does not have to be a formal education, but simply a call to be as educated as possible on the issues of importance. Our present world has the most extensive resource in finding information about anything anyone would ever want to know. This reaches much further than medicine, it is applicable to technology, business, politics, and sociology, to name a few. A person who wants to make a difference does not have to be an expert, they only have to be willing to learn and to teach those who are not educated.

Increased awareness will open up worlds of possibilities. Even coming to terms with the fact that cancer seems to be more prevalent today because medical advances have kept people from dying in other situations is a beginning. The hospital delivery room and the influenza vaccine have saved countless lives during childbirth and flu season. It is also important to recognize that there are increased carcinogens in our environment and decreased health in developed countries that contribute to increasing cancer rates.

A large portion of the population will is asking for a cure for cancer, a magic bullet that will stop all suffering. This is not an easy subject, and this is not something that will exist in the same sense that allowed for the polio vaccine. We've gone through great lengths to oversimplify "a cure for cancer," something that definitely should not be oversimplified. What would this even mean? Improving cancer treatment so that the survival rate is 100%? Developing a method of editing genes to avoid cancer altogether?

Perhaps one improvement will involve humans becoming more accepting of our inevitable death, to remove this fear of the unknown and focus on what is truly important.

This disease is complex in everything but its root nature. It affects different organs, results in different symptoms, requires different treatment, and can be caused by different things. How cancer will manifest itself is different in each and every patient. Cancer is an undeniably complicated disease, but that should not prevent any person from being able to have a basic understanding. As with any subject, it can be broken down into its component parts and the understanding can be built from the ground up. This work is one version of an everyday guide to cancer. On another day we can create a layman's guide to electronics?

REFERENCES

INTRODUCTION

1 U.S. Cancer Statistics Data Visualizations Tool, based on November 2017 submission data (1999-2015): U.S. Department of Health and Human ……..Services, Centers for Disease Control and Prevention and National Cancer Institute; www.cdc.gov/cancer/dataviz, June 2018.

2 Scheider, Conrad, and Jacqueline Guyol. “Maine Voices: As the 'Tailpipe of the Nation,' Maine Deserves Cleaner Air.” *Portland Press Herald*, 17 Oct. 2017.

3 Walsh, Tom. “Age, Lifestyle Contribute to High Cancer Rate in Maine.” *Bangor Daily News*, 2 May 2013.

4 Arora, Neeraj K., et al. “Frustrated and Confused: The American Public Rates Its Cancer-Related Information-Seeking Experiences.” *Journal of General Internal Medicine*, vol. 23, no. 3, 2007, pp. 223–228., doi:10.1007/s11606-007-0406-y.

PART I:

THE CELLS THAT WORK TOO WELL

5 “Lifetime Risk of Developing or Dying From Cancer.” *American Cancer Society*,

4 Jan. 2018, www.cancer.org/cancer/cancer-basics/lifetime-probability-of-developing-or-dying-from-cancer.html.

6 Avissar, Yael, et al. *Biology*. OpenStax College, Rice University, 2016.

7 Alberts, Bruce, et al. *Essential Cell Biology*. Garland Science, 2014.

PART II:

AN UNNATURAL HISTORY

8 Mukherjee, Siddhartha. *The Emperor of All Maladies*. Scribner, 2010.

9 "About Cancer." *National Cancer Institute*, National Institute of Health, 23 Dec. 2015, www.cancer.gov/about-cancer/causes-prevention/risk.

10 "Cancer Screening." *National Cancer Institute*, National Institute of Health, 9 Apr. 2018, www.cancer.gov/about-cancer/screening.

11 "Types of Cancer Treatment." *National Cancer Institute*, National Institute of Health, 29 Apr. 2015, www.cancer.gov/about-cancer/treatment/types.

12 Devita, Vincent T., and Edward Chu. "A History of Cancer Chemotherapy." *Cancer Research*, vol. 68, no. 21, 1 Nov. 2008, pp. 8643–8653., doi:10.1158/0008-5472.can-07-6611.

13 Freeman, Matthew D., et al. "The Evolution of Mastectomy Surgical Technique: from Mutilation to Medicine." *Gland Surgery*, vol. 7, no. 3, 7 June 2018, pp. 308–315., doi:10.21037/gs.2017.09.07.

14 Gianfaldoni, Serena, et al. "An Overview on Radiotherapy: From Its History to Its Current Applications in Dermatology." *Open Access Macedonian Journal of Medical Sciences*, vol. 5, no. 4, 25 July 2017, pp. 521–525., doi:10.3889/oamjms.2017.122.

15 "Immunotherapy." *National Cancer Institute*, National Institute of Health, 28 Nov. 2018, www.cancer.gov/about-cancer/treatment/types/immunotherapy.

16 “What Are Genome Editing and CRISPR-Cas9? - Genetics Home Reference - NIH.” *U.S. National Library of Medicine*, National Institutes of Health, 30 Aug. 2017, ghr.nlm.nih.gov/primer/genomicresearch/genomeediting.

PART III:

BY THE NUMBERS

17 Geraci, John, et al. “What Teens Want From Their Schools: A National Survey of High School Student Engagement.” *Thomas B. Fordham Institute*, 27 June 2017.

18 Kent, Jon. “An Insider’s Guide to Choosing a Cancer Charity.” *Medium*, 1 Apr. 2018.

19 “Contributing to Cancer Research.” *National Cancer Institute*, National Institute of Health, 30 Apr. 2018, www.cancer.gov/about-nci/overview/contributing.

20 “Budget and Appropriations.” *National Cancer Institute*, National Institute of Health, 3 Oct. 2018, www.cancer.gov/about-nci/budget.

21 HHS Office of the Secretary,Office of Budget, and Ob. “FY 2018 Budget in Brief - NIH.” *HHS.gov*, US Department of Health and Human Services, 23 May 2017, www.hhs.gov/about/budget/fy2018/budget-in-brief/nih/index.html.

22 “Annual Reports & Financial Statements.” *Susan G. Komen®*, ww5.komen.org/AboutUs/FinancialInformation.html.

23 “Crunching Numbers: What Cancer Screening Statistics Really Tell Us.” *National Cancer Institute*, 16 July 2018, www.cancer.gov/about-cancer/screening /research/what-screening-statistics-mean.

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