Should Chemotherapy Continue to be Used as Treatment for Cancer?

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On my honor as a University Student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments

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## Introduction

Cancer is the second leading cause of death in the United States, surpassed only by heart disease. The American Cancer Society estimates that in 2023, over 1.9 million Americans will be diagnosed with cancer, and approximately 609,820 cancer-related deaths will occur, equivalent to about 1,670 deaths per day (American Cancer Society, 2023). Currently, there are no widely recommended screening tests for cancer. Instead, patients typically receive a diagnosis when they present signs or symptoms (American Cancer Society, 2020). Unfortunately, most cancers have significantly impacted the patient's quality of life by the time they are detected.

Cancer is a group of diseases characterized by the uncontrolled growth and spread of abnormal cells and can be fatal if left untreated. Chemotherapy (or "chemo") is one of the most common types of cancer treatment and works by destroying fast-growing cells. However, as chemotherapy does not target specific cells, it can irreversibly harm other healthy, fast-growing cells in the body (Miller, 2022). As a result, eradicating healthy cells alongside cancer cells is likely to manifest as adverse reactions or side effects. Furthermore, since each person's body responds differently to treatment, it is difficult for doctors to predict how the body will react.

In this paper, we will explore the history behind chemotherapy to determine if alternative cancer treatments should be used instead, given the physical, mental, and emotional toll these therapies can have on cancer patients and their families.

## Methods

Case studies were the most helpful framework for exploring the complexities of cancer treatment and its impact on patients. In addition, I used history, philosophy, and personal anecdotes to provide a broader context for understanding cancer treatment. Finally, I utilized the Actor-Network Theory to understand the interactions between patients and their treatments.

One important framework used in this field is SWOT (Strengths, Weaknesses, Opportunities, and Threats) analysis, which evaluates the internal and external factors that may affect the success of a treatment approach. By identifying the strengths and weaknesses of the approach, as well as the opportunities and threats in the external environment, I was able to examine both the unique mechanisms and side effects of the approach and the potential opportunities and threats presented by other treatments.

# **Results & Analysis**

# Cancer Background

Cancer remains a devastating disease both physically and emotionally, but it is not a recent disease. The oldest descriptions of what is now recognized as cancer were found in Egypt, dating back to about 3000 BC (American Cancer Society, 2018). Despite people living longer, thus increasing their risk of getting cancer, the data shows that even after accounting for this, the cancer rate is still increasing (Roser & Ritchie, 2015). Abnormal cell growth that invades surrounding tissues and spreads to other organs primarily causes cancer, leading to morbidity and mortality in patients. The human body, which consists of trillions of cells, is susceptible to cancer that can originate from almost any part of the body. Normally, human cells grow and multiply to form new cells as needed by the body. However, sometimes this orderly process breaks down or is damaged, allowing abnormal cells to grow and multiply uncontrollably. Chemotherapy, or

chemical therapy, is a standard cancer treatment that involves using cytotoxic (toxic to cells) drugs to kill cancer cells. Researchers have found that giving combinations of drugs enhances the cancer-killing effect, so they often administer them together or sequentially. Despite the widespread use of chemotherapy, some may question if the benefits outweigh the potential drawbacks.

### Chemotherapy Background

Inspired by World War II, scientists developed chemotherapy as a method of chemical warfare on cancer cells. During an air raid, hundreds of tons of mustard gas were released on the Bari harbor in Italy, leading to the decimation of normal white blood cells in the body (Mukherjee, 2010, p. 433). This discovery led pharmacologists to consider using a similar chemical to kill the cancers of white blood cells. In the 1940s, the nitrogen mustard compound found in mustard gas was studied and found to work against a cancer of the lymph nodes called lymphoma, leading to an era of chemotherapy enthusiasm. However, during this period, doctors and scientists were so focused on finding the perfect chemotherapy treatment for different types of cancers that they were often oblivious to or in denial of the daunting side effects and the toll these treatments had on patients.

## Case Studies

The 4-drug VAMP (Vincristine Sulfate, Adriamycin, Methotrexate, and Prednisone) chemotherapy regimen, introduced in 1961 for treating leukemia in children, was initially feared due to its potential to cause death by infection (Mukherjee, 2010, p. 152). Due to the chemotherapy's suppression of white blood cells, patients were left weak and unable to fight off harmful microorganisms, often requiring ventilation. However, after several weeks, many patients began to recover and experienced remissions with undetectable leukemia. The trial's results were remarkable and helped to persuade even the previously skeptical to support it. Unfortunately, remission was not permanent for most patients, and relapses proved fatal for all except 5%. Out of the fifteen patients treated, only two survived. Still, doctors use this 4-drug combination chemotherapy regimen today to treat children with low-risk Hodgkin lymphoma, an immune system cancer (NIH: National Cancer Institute, 2011).

The success of the VAMP regimen as the first systematic cure of cancer with drugs, despite its severe side effects, was seen as a groundbreaking achievement that fueled the enthusiasm for cytotoxic chemotherapy. The MOPP (Mechlorethamine, Oncovin, Procarbazine, and Prednisone) regimen was another early attempt at combining several active agents, which also showed remarkable success. The lead on the study, Vincent DeVita, expressed his astonishment when their sickest patient with Hodgkin's lymphoma went into remission from this regimen, but the success persisted. The advent of multiple-drug chemotherapy dramatically changed the prognosis of patients previously untreated in the more severe stages of Hodgkin's disease (DeVita & DeVita-Raeburn). DeVita and his colleagues' MOPP regimen increased the cure rate for advanced Hodgkin's disease from close to zero to over 70%. Today, the cure rate for Hodgkin's lymphoma is around 90% (Workman, 2016).

### John Cleland

In 1973, John Cleland received a diagnosis of testicular cancer that had spread to his lymph nodes and lungs, with a survival rate of less than five percent. He began treatment in the cancer ward at Indiana University with a toxic three-drug regimen derived from these studies conducted in the 1960s. Cleland's health deteriorated due to the treatment, and he spent a significant amount of time in and out of the hospital without experiencing any success in the treatment. One day, when his wife suggested they go outside to enjoy the afternoon, Cleland realized he was too weak to stand up. Upon realizing this, he felt immense shame and embarrassment as he broke down in tears while hospital staff had to carry him back to his bed. Over that next year, Cleland decided to take the gamble with a new combination of drugs and enrolled as "patient zero" for BVP (regimen containing bleomycin, vinblastine, and cisplatin). Cleland was one of twenty other patients whose tumor vanished with the onset of this regimen.

According to Mukherjee's *The Emperor of All Maladies* (2010, p. 192), after this success of cisplatin-based chemotherapy, there was a push for testing the drug on thousands of cancer patients across America. Cisplatin became ubiquitous in cancer wards, with patients often experiencing intense nausea and vomiting up to twelve times a day. Despite these debilitating side effects, oncologists were determined to find a cure for cancer and believed that every poison could be a potential drug. This mindset led to a flood of chemicals being tested by the NCI (National Cancer Institute), often discovered by accident and with little regard for their indiscriminate cytotoxic effects. As a result, the process was said to become a trial and error on a massive human scale, sometimes with disastrous consequences. As more combination drugs entered clinical trials, Rose Kushner, a National Cancer Advisory Board member, warned against the growing disconnect between doctors and their patients. She noted that doctors talked about life-threatening side effects but often failed to acknowledge less severe but still significant side effects, such as breaking blood vessels in the eyes due to intense vomiting. She criticized the smiling oncologists who were unaware of the harsh realities their patients were experiencing.

# Robert Pope

In 1982, Robert Pope was diagnosed with advanced Hodgkin's disease after graduating from the Nova Scotia College of Art and Design. He recounts his experience in his book *Illness and Healing: Images of Cancer* (1991/2008). Although most patients with this disease have a

75% chance of survival, Pope's case was more severe. During the 7-month MOPP chemotherapy regimen, Pope experienced increasingly severe side effects that overshadowed his illness. Vomiting for up to five hours and experiencing severe nausea for several days afterward became a constant presence in his life. The chemotherapy also destroyed his normal blood cells, causing dangerous drops in his blood count that led to delays in his treatment. Support from family and the hope for a cure were the two things that helped him the most during this difficult period.

After completing the 7-month MOPP treatment, Pope was in complete remission, but cancer reappeared in his neck after four months. The doctors immediately suggested another 6-month cycle of chemotherapy using four different drugs (ABVD). Pope found this experience to be the worst period of his life, with even more severe side effects than before. He was in so much pain that he felt like dying and had to be forced by his family to go to the hospital for injections. As his blood counts dropped again and the doctors delayed his treatment, he experienced increasing isolation, with fewer visits from friends.

Pope finished this second round of chemotherapy, which was even more arduous than the first. However, the cancer returned after six months, spreading to his abdomen and lowering his chance of survival to less than 20%. His only hope was radiation therapy, which used X-rays to target specific areas of the body affected by cancer. However, because cancer cells are not entirely separate from healthy cells, the radiation also destroys nearby healthy tissues. Pope received forty radiation treatments, which permanently destroyed two-thirds of his bone marrow. The doctors were concerned about missing any cancer cells, as even one remaining cell could cause treatment failure. Despite the physical toll, he again credits the support of his family and friends for helping him make it through the treatments.

During his battle with cancer, Pope used painting to explore the emotional and physical toll of illness. His paintings, known for their vivid colors and layered imagery, centered on the human body and the themes of illness and healing. In his book *Illness and Healing: Images of Cancer*, Pope compiled a collection of his paintings and reflections on his experience with cancer, exploring topics such as pain, suffering, and finding meaning in the face of death. While the series moves chronologically from illness to healing, the paintings do not always present positive, uplifting images. Many depict cancer patients as alone and alienated from a society that stigmatizes their illness. In one painting, "Chemotherapy," a woman is depicted as fearful and reluctant as she stares at the syringe that may save her life. Pope's book has received critical acclaim and is used in medical schools and art therapy programs to explore the emotional and psychological dimensions of illness.

Faced with the reality of death after he underwent the radiation treatments, Pope decided to take responsibility for his healing by exploring alternative therapies and doing everything he could while he still had strength. With the teachings of Dr. Anthony Sattilaro in his book *Recalled By Life*, Pope turned to nutrition and lifestyle, which helped him live ten years without cancer. Sadly, he died in 1992, at age 35, from the effects of chemotherapy and radiation (Carlson, 1992).

### Discussion

In the early days of chemotherapy development, surgery, the traditional method for combating cancer, was considered primitive, indiscriminate, and exhausting. The aim became to launch a large-scale attack with chemotherapy to eradicate cancer, but this approach had its drawbacks. Using cytotoxic drugs to destroy the immune system could cause permanent sterility and lead to the emergence of peculiar infections, exposing the dual-edged sword nature of cytotoxic chemotherapy (Meistrich, 2013). Moreover, chemotherapy can be an arduous experience, posing physical, mental, and financial challenges. Nevertheless, some patients are willing to endure the horrors of treatment to remain cancer-free. Unfortunately, the side effects of chemotherapy and radiation therapy, sometimes fatal, tend to manifest in patients 6 to 12 years after treatment. Still, cancer may return for others, forcing them, their families, and friends to endure agonizing cycles of unsuccessful chemotherapy, all while desperately hoping for a cure. The unsystematic nature and debilitating side effects of chemotherapy have spurred a fervent search for alternative treatments.

# **Alternative Treatments**

Before the 1980s, two fundamental vulnerabilities of cancer cells formed the foundation of cancer therapy: 1) most cancers started as local diseases before spreading systemically, and 2) the rapid growth rate of cancer cells. Radiation therapy exploits the first vulnerability of cancer cells by using X-rays to sear the cancer cells with localized energy. In contrast, chemotherapy drugs target the second vulnerability by starving or thwarting all cell division. However, as mentioned previously, these two vulnerabilities can only be targeted to a point as they fail when cancer cells have spread beyond the limits of what can be irradiated and hinder the growth of healthy, normal cells.

Interestingly, cancer rates can change dramatically in and within different regions worldwide. Based on this observation, Dr. David Prescott and Dr. Abraham S. Flexer suggest in their book, *Cancer: The Misguided Cell*, that changes in environment, diet, and lifestyle could prevent up to 90% of all human cancer, based on this observation.

## Prevention

According to the World Health Organization (WHO), 30-50% of all cancer cases are preventable. Therefore, emphasizing prevention strategies is recommended to manage cancer and reduce long-term costs effectively. Perhaps the best example to highlight this is the widespread recognition, beginning in the 1930s, of the link between smoking and lung cancer. Tobacco smoke poses a significant health risk, with more than 7,000 chemicals, at least 250 of which have adverse effects on health, and 69 identified as cancer-causing agents. The World Health Organization (2023) estimates that smoking is responsible for about 85% of all lung cancer cases worldwide, making it the leading avoidable risk factor for cancer-related deaths (see Figure 1). Unfortunately, tobacco is more addictive than heroin, so addictive that 64% of smokers diagnosed with cancer continue even after they learn they have the disease.



Figure 1: Despite accounting for only 13% of new cancer cases, lung and bronchus cancer are nearly a quarter of cancer deaths (USAFacts, 2023).

The American Cancer Society outlines some of the most important steps to reduce a person's cancer risk, including 1) controlling one's weight, 2) being physically active regularly, 3) following a healthy eating pattern, and 4) avoiding or limiting alcohol. Being overweight and obese increases the chance of cancer cells developing since fat cells produce more hormones,

growth factors, and inflammation that cause cells in the body to divide more often (World Cancer Research Fund / American Institute for Cancer Research, 2018). Being active and following a healthy eating pattern can help reduce the risk of cancer by helping with weight control and limiting the ingestion of potentially harmful processed substances. Finally, similarly to obesity, alcohol can make cells more likely to divide. Alcohol can also damage cells and make it easier for mouth and throat cells to absorb cancer-causing chemicals. Drinking alcohol is one of the most significant risk factors for breast cancer, but it can also increase the risk of mouth, throat, liver, and bowel cancer (Roser & Ritchie, 2015/2019).

Although there are no certainties when aiming to prevent cancer, studies indicate that adopting healthy lifestyle habits can significantly reduce the risk of developing the disease. As Benjamin Franklin famously said, "An ounce of prevention is worth a pound of cure." Prevention can not only preserve lives and relationships but also save costs. Nevertheless, prevention alone cannot eliminate cancer since some risk factors, like genetics, are beyond an individual's control.

# Targeted Therapy

During the 1980s, advances in cancer biology led to the realization that the challenge of therapy was to identify slight differences between normal and cancer cells in terms of their genes, pathways, and acquired capabilities and therefore develop a targeted weapon that could accurately strike at these differences (Mukherjee, 2010, p. 369). Targeted molecular therapy is a personalized approach to cancer treatment tailored to meet each individual's specific needs because cancer development varies in the body. Since targeted therapy allows medical oncologists to customize cancer treatment more precisely, the benefits include potentially causing less harm to normal cells, leading to fewer side effects, and increasing effectiveness,

ultimately resulting in an improved quality of life for the patient. The National Cancer Institute at the National Institutes of Health (2022) asserts that the complex nature of cancer means that although some cancers have identifiable molecular targets, researchers are still discovering new targets. Even the same type of cancer can exhibit different molecular targets. Another challenge is that cancer cells can evolve to become resistant to targeted therapy, rendering it ineffective. Resistance can occur due to changes in the target or the development of alternative growth pathways that do not rely on the target. To combat resistance, targeted therapy may need to be combined with other treatments like chemotherapy and radiation or even multiple types of targeted therapies.

In the 1990s, Dr. Brian Druker, a researcher at Oregon Health and Science University, sought a treatment for chronic myelogenous leukemia (CML) that could specifically target cancer cells while sparing healthy cells, unlike traditional chemotherapy (NIH: National Cancer Institute, 2018). Through extensive research, he and his partner identified a drug that was incredibly good at killing CML cells–imatinib (Gleevec). Five years after the phase 1 clinical trial, 98% of the patients from the trial were still in remission. As a result, imatinib was approved by the FDA in 2001 for the treatment of chronic myelogenous leukemia (CML). Imatinib is still used as a standard treatment for CML and has significantly improved the prognosis for patients with this type of cancer. In fact, someone with CML who achieves remission after two years of imatinib treatment has a similar life expectancy to someone who does not have cancer. The discovery and development of imatinib also helped pave the way for a new class of cancer drugs called targeted therapies. These drugs target cancer cells with specific genetic abnormalities while sparing healthy cells. Unlike chemotherapy, which can affect healthy cells as well as

cancer cells, targeted therapies have fewer side effects and can be more effective in treating certain types of cancer.

Since the beginning of the 21st century, small-molecule drugs that target specific tumorigenic (capable of forming tumors) proteins have been available to treat different types of cancer. These proteins, called tyrosine kinases, have been linked to the development of several cancers, including leukemia, lung cancer, breast cancer, pancreatic cancer, and gastrointestinal stromal tumors (GISTs). Drugs that target these proteins have various benefits over traditional chemotherapy, including reduced systemic toxicity and the ability to be taken orally (Culhane & Li, 2008).

Katie Pope Kopp underwent numerous cycles of chemotherapy and a stem cell transplant to combat her non-Hodgkin lymphoma (Stein, 2022). However, despite these efforts, the cancer persisted. Five years later, Kopp was introduced to a novel approach to cancer treatment using CRISPR, a gene-editing technique. Recently, some medical professionals have begun to use CRISPR to modify immune system cells to treat cancers such as hers. Kopp received the experimental CRISPR gene-editing treatment more than a year ago and remains in remission. This raises hope that the gene-editing technique may offer new hope to some cancer patients.

We have entered a new era that looks to more targeted methods for cancer treatment. As our understanding of the human genome and cancer biology expands, we can offer more effective solutions to cancer patients who may not benefit from chemotherapy. This progress also offers hope for moving beyond chemotherapy's less specific and often debilitating effects.

### Conclusion

In the face of his grueling cancer treatments, artist Robert Pope observes that our approach to cancer reveals much about our cultural values. The language we use to describe the disease is often aggressive and violent, with talk of a "war on cancer" and cancer cells "invading" and "colonizing" the body. Both medical and political sectors frequently compare chemotherapy to chemical warfare, where doctors subject patients to toxic substances that sap their physical strength and resolve. As Weinberg (2014, p. 797) notes, many of the current anti-cancer therapies were developed in 1975, when our understanding of the genetic and biochemical mechanisms driving cancer was limited. However, as we continue to delve deeper into these mechanisms, we have the potential to provide more effective treatments that are less burdensome and have a more positive impact on patients' quality of life.

## References

American Cancer Society. (2018, January 4). Understanding What Cancer Is: Ancient Times to Present. Cancer.org; American Cancer Society, Inc.

https://www.cancer.org/treatment/understanding-your-diagnosis/history-of-cancer/what-is -cancer.html

American Cancer Society. (2020, May 5). Can Brain and Spinal Cord Tumors in Adults Be Found Early? Cancer.org.

https://www.cancer.org/cancer/types/brain-spinal-cord-tumors-adults/detection-diagnosis-staging/detection.html

American Cancer Society. (2023). Cancer Facts & Figures 2023. American Cancer Society.

- Carlson, T. (1992). *Turning sickness into art: Robert Pope and his battle with cancer* (pp. 229–232). CMAJ : Canadian Medical Association journal.
- Culhane, J., & Li, E. (2008, October 17). *Targeted Therapy with Tyrosine Kinase Inhibitors*. USpharmacist.com; Jobson Medical Information LLC.

https://www.uspharmacist.com/article/targeted-therapy-with-tyrosine-kinase-inhibitors

- DeVita, V. T., & DeVita-Raeburn, E. (2015). The Death of Cancer. Sarah Crichton Books.
- Meistrich, M. L. (2013). The Effects of Chemotherapy and Radiotherapy on Spermatogenesis in Humans. *Fertility and Sterility*, *100*(5). https://doi.org/10.1016/j.fertnstert.2013.08.010
- Miller, R. (2022, May). Side Effects of Chemotherapy and Radiation (for Parents) Nemours KidsHealth. Kidshealth.org. https://kidshealth.org/en/parents/side-effects.html

Mukherjee, S. (2010). *The Emperor of All Maladies: A Biography of Cancer* (pp. 186–433). Scribner.

- NIH: National Cancer Institute. (2011, December 22). VAMP. Www.cancer.gov. https://www.cancer.gov/about-cancer/treatment/drugs/vamp
- NIH: National Cancer Institute. (2018, April 11). How Gleevec Transformed Leukemia Treatment. National Cancer Institute; Cancer.gov. https://www.cancer.gov/research/progress/discovery/gleevec
- NIH: National Cancer Institute. (2022, May 31). *Targeted Therapy*. National Cancer Institute; Cancer.gov. https://www.cancer.gov/about-cancer/treatment/types/targeted-therapies
- Pope, R. (2008). *Illness & Healing: Images of Cancer* (25th Anniversary). Hantsport Lancelot. (Original work published 1991)
- Roser, M., & Ritchie, H. (2015). Cancer. *Our World in Data*. https://ourworldindata.org/cancer#is-the-world-making-progress-against-cancer
- Stein, R. (2022, December 13). CRISPR gene-editing may boost cancer immunotherapy, new study finds. NPR.org.

https://www.npr.org/sections/health-shots/2022/12/13/1140384354/crispr-improves-cance r-immunotherapy-car-t-cell

USAFacts. (2023, January 20). US cancer rates and trends: How have cancer rates and mortality changed over time? USAFacts.

https://usafacts.org/articles/how-have-cancer-rates-changed-over-time/

Workman, P. (2016, February 4). *The death of cancer? Part 1: the birth of effective drug therapy*. The Institute of Cancer Research (ICR).

https://www.icr.ac.uk/news-features/latest-features/the-death-of-cancer-part-1-the-birth-of -effective-drug-therapy World Cancer Research Fund / American Institute for Cancer Research. (2018). Diet, Nutrition, Physical Activity and Cancer: a Global Perspective. World Cancer Research Fund International.

World Health Organization (WHO). (2023). Preventing cancer. WHO.

https://www.who.int/activities/preventing-cancer