

Chemotherapy/Radiation Causes Leukemia in Cancer Patients.

Collecting and Storing Immune and Stem Cells to Prevent or Reduce Cancer Risks.

The battle against cancer is a winnable endeavor. With modern advances in treatment, increased awareness, and developments in early detection, the survival rate for patients diagnosed with cancer is rising. This increased survival rate however, comes with increased risks and incidences of long term complications, such as leukemia.

On June 11 2012, "Good Morning America" co-host Robin Roberts, who was previously diagnosed with breast cancer in 2007, announced that she was facing her second major health battle in just five years. Roberts, age 51, was diagnosed with myelodysplastic syndrome (MDS)¹. MDS is a rare and often fatal blood disease in which the bone marrow has lost its ability to produce enough mature blood cells, such as white blood cells to fight infection and red blood cells to transport oxygen to different parts of the body. MDS following chemotherapy and/or radiation often transforms into leukemia, a life-threatening blood cancer.

In 2018, Roberts celebrated six years since her lifesaving bone marrow/stem cell transplant, what she considered to be her sixth "birthday".

Treatment-related MDS and Acute Myeloid Leukemia (t-MDS/AML) are Significant and Serious Complications of Prior Cancer Therapy

Roberts had received chemotherapy and radiation therapy to treat her early-stage breast cancer in 2007.

T-MDS/AML as a side effect of chemotherapy and/or radiation is well documented and may not be clearly explained to patients at the time of diagnosis and treatment planning. When compared to available population incidence data SEER (Surveillance, Epidemiology, and End Results), an 11 times higher rate of MDS and 5 times higher rate of AML was observed among breast cancer patients aged less than 65 years, who had been previously treated with radiation and chemotherapy.²

This increased risk of leukemia following chemotherapy occurs in all types of cancers. In a large study of 426,068 adults, initially treated with chemotherapy for a primary malignancy (9 US population-based cancer registries, 1975-2008), the incidence of AML cases was 5 times more than expected in the general population.³

More recently, in a 2018 publication of a population-based study of 700,612 adults in a US cancer data registry, the risk of tMDS/AML was significantly increased to greater than 10-fold.⁴ This was the case after chemotherapy for 22 of 23 solid cancer types investigated (all except colon cancer). Therefore, gains in cancer survival from modern treatment approaches have to be balanced against tMDS/AML risks and other chemotherapy-related adverse effects. This requires continued efforts to develop effective agents

and cancer treatments with fewer late side effects. Proactive approaches are needed to educate patients about the risks and to provide interventions to minimize and prevent tMDS/AML and cancer risks.

(T-MDS/AML) that is a Consequence of Past Chemotherapy Can be Harder to Treat than MDS Unrelated to Chemotherapy/Radiation

Patients with t-MDS/AML are often resistant to the conventional therapies used for those cases of MDS/AML which do not occur as a result of chemotherapy and radiation.⁵ They are usually unable to tolerate the intensive chemotherapy used to treat MDS/AML, because of the increased toxicity caused by their previous exposure to chemotherapy and radiation. The treatment outcomes for patients with t-MDS/AML are poor with shorter survival times than for patients with MDS/AML unrelated to chemotherapy and radiation.⁵ As a result there are very few treatment options for t-MDS/AML.

Roberts received an allogeneic (from a donor) bone marrow/stem cell transplant from her older sister in 2012, a procedure that necessitated her taking several months' leave from "Good Morning America". Allogeneic bone marrow/stem cell transplantation is a risky and complicated procedure and carries a risk of death in the range of 23 to 61 percent, and the chance of overall survival from this transplant ranges from 22 to 38 percent.⁶

Allogeneic stem cell transplantation (SCT) is regarded as the treatment of choice for the majority of young patients with t-MDS/AML who have a human leukocyte antigen (HLA)-compatible donor (stem cells are obtained from a sibling or unrelated donor sourced from a national marrow donor registry).⁶ Robert's sister was a suitable donor and she was fortunate because this occurs in only 25-30% of searches in siblings. For patients lacking an (HLA)-compatible donor, chemotherapy followed by autologous SCT (stem cells obtained from the same patient) or an identical twin may be reasonable alternatives.^{7, 8} A substantial number of candidates may not be eligible for an autologous SCT, due to failure to induce remission or failure to collect sufficient numbers of stem cells.

Many Patients with t-MDS/AML will not have a Suitable Genetic Matched Donor

An optimal or perfect donor for allogeneic transplantation will match the patient at the *HLA-A*, *HLA-B*, *HLA-C*, and *HLA-DRB1* loci (i.e., an 8/8 high-resolution HLA match).

Many patients will not have an optimal donor. The likelihood of finding an available donor from the national marrow registries varies among racial and ethnic groups, with the highest among whites of European descent (51%), the lowest among black Americans of all ethnic backgrounds (16 to 19%) and intermediate for Hispanics, Asians, Pacific Islanders, and Native Americans at 28%.⁹ For the majority of patients with treatment-related MDS, there are no suitable options or at worst a mismatched donor transplant with a high mortality risk and complications such as graft versus host (an autoimmune disease where the donors' immune cells attacks the tissues of the patient).

Proactive Approaches are needed to Educate Patients about the Risks and to Provide Interventions to Minimize and Prevent tMDS/AML and Cancer Risks

Proactive Approach: Collect and store the patient's own stem cells before receiving chemotherapy and radiation therapy for cancer:

At the Maharaj Institute of Immune Regenerative Medicine (The Institute) in Boynton Beach, Florida, a unique service is provided for cancer patients. Prior to receiving chemotherapy and radiation therapy cancer patients can have their stem cells, as well as immune cells collected and stored for future use.

By storing and freezing their bone marrow stem cells in the Stem Cell Cryobank, cancer patients can be proactive and save some of their stem cells from being damaged by their subsequent chemotherapy and radiation therapy.

Patients might think that there is no value in storing their cells after a diagnosis of cancer, because their immune system is already compromised and maybe that is why they developed cancer in the first place. However, the process of releasing stem cells from the bone marrow (called stem cell mobilization) prior to collecting them from the blood, increases the immune cells by 7 to 14 fold in addition to a 200 to 400 fold increase in stem cells.¹⁰ These stem cells can be used for a bone marrow/stem cell transplant at a later date. This is similar to a transplant between twins, which has outcomes of disease free survival and overall survival equivalent to a matched related or unrelated transplant.⁸ It is a solution for the problem of having to find a donor at a later date, if treatment-related MDS or leukemia develops, and to avoid the high mortality and graft versus host disease of an allogeneic transplant.

Also, there are constant developments of newer immunotherapies, such as chimeric antigen receptor (CAR) T Cells using genetically modified T cells for treatment of blood cancers and other types of cancers. However, a limitation of (CAR) T cell therapy is that the numbers of stem cells and immune cells are low when they are collected after the cancer patient has received chemo/radiation therapy, and at the onset of the treatment-related MDS/ leukemia, or the re-occurrence of the original cancer. This problem is avoided in the cancer patient who has proactively collected and stored their immune and stem cells which are in high numbers before chemotherapy/ radiation and therefore more useful for (CAR) T cell therapy.

Proactive Approach: Collecting and storing Stem cells can be beneficial for people at risk of cancer or chronic diseases; it's for anyone who wants to store healthy immune cells:

SEER cancer incidence data shows that approximately 39.3 percent of men and women will be diagnosed with cancer of any site at some point during their lifetime, based on 2014-2016 US data. In 2019, it is estimated that there will be 1,762,450 new cases of cancer of any site and an estimated 606,880 people will die of this disease. The most common type of cancer is breast cancer, with 271,270 new cases expected in the United States in 2019. The next most common cancer is lung cancer followed by prostate cancer.¹¹ Despite how overwhelmingly widespread cancer has become in the United States, researchers are making substantial progress in the treatment of certain cancers. However, an increasing number of

health minded individuals are anxious to avoid these risks and become another cancer statistic. They proactively work to reduce their risk for cancers, to identify cancers before they become symptomatic when treatments are most effective and to measure and maintain a normal immune system.

Measure and Maintain a Normal Immune System

As we age, our immune system gradually weakens over time. Starting around the age of 30 our immune systems are in a slow gradual decline until somewhere between the ages of 65-74. At that point, our immune system takes a significant drop.

Health conscious individuals or cancer patients can measure their immune systems with a blood test. While many blood tests such as a Complete Blood Count (CBC) may be normal, there are abnormalities within the immune system that do not show up on these regular diagnostic tests.

Measuring the immune system gives an indicator as to the body's ability to fight cancer and other diseases. By being aware of the state of the immune system, individuals can prevent its weakening by modifying their life-style and environmental exposures..

To measure how well your immune system is functioning, at The Maharaj Institute a sophisticated blood test is used to examine the innate and adaptive parts of the body's immune system which includes an extensive array of cellular blood markers. This process examines cells that standard blood tests do not and creates an Immune Risk Profile (IRP) that can range from – no abnormalities – through mild, moderate and severe.

Those with a healthy immune system can collect and store their stem cells in case they are needed to restore their immune health in the future.

For those individuals with an abnormal immune system, a root cause analysis can identify possible causes for the weakened immune system. Once the deficiencies are corrected, the procedure continues with the gathering and storage of adult stem cells mobilized from the bone marrow followed by a maintenance plan to keep the immune system on track. These are solutions that address the root cause of the individual's problems, with a focus on proactive measures to safeguard their health and longevity. The best tools a person can have in their wellness toolbox is a healthy immune system and a second one in the Stem Cell Cryobank.

With an impaired immune system, cancer survivors are at an elevated risk for other types of cancer and illnesses. They can benefit from these proactive measures to correct the deficiencies, have a maintenance plan and bank and store their stem cells and improved immune system.

When reintroduced into a health-challenged body, adult stem cells mobilized from the bone marrow have the remarkable potential to repair the immune system and to develop and grow into many different specialized cell types¹². They circulate through the blood helping to repair tissue and organ damage.

As the benefits for stem cell therapy evolves, so will the number of uses that are available for an individual's banked stem cells. With more than 3,000 U.S. Clinical Trials using adult stem cell therapies, there is growing evidence to show that an individual's own stem cells have the capability for growth, repair, and regeneration of damaged tissue and cells in the body. Currently there are more than 80 medically accepted uses for adult stem cells mobilized from the bone marrow including the treatment of many blood cancers, bone marrow failures, and immune disorders.

Ideally, everyone should have a healthy Immune System stored for the future.

For more information on measuring as well as collecting and storing your Immune System, please contact the Maharaj Institute of Immune Regenerative Medicine at **561-752-5522 or info@miirm.org**.

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