

# Exploring Cardiovascular, Endocrine and Neurocognitive Late Effects in Neuroblastoma Survivors

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## Introduction

Neuroblastoma, a common pediatric cancer, primarily affects children under the age of 5 and arises from the sympathetic nervous system, often in the adrenal glands or along the spine. Over the past few decades, advancements in treatment modalities—such as chemotherapy, surgery, radiation therapy and stem cell transplants—have significantly improved survival rates. Despite these advancements, an increasing number of neuroblastoma survivors face long-term health challenges known as "late effects." These are chronic conditions or disabilities that arise months or even years after cancer treatment has ended. The three main categories of late effects often observed in neuroblastoma survivors are cardiovascular, endocrine and neurocognitive health issues. Understanding and managing these late effects is crucial in ensuring the continued well-being of neuroblastoma survivors as they transition from pediatric to adult care [1].

## Description

Cardiovascular complications represent a significant concern for cancer survivors, particularly those treated with anthracyclines, radiation therapy, or a combination of both. Neuroblastoma survivors who have undergone these treatments are at heightened risk of developing cardiovascular issues later in life. Anthracyclines, a class of chemotherapy drugs frequently used in the treatment of neuroblastoma, are known to cause damage to heart muscle cells. This damage can result in cardiomyopathy, a condition where the heart becomes weakened and is unable to pump blood efficiently. Over time, this can progress to heart failure, where the heart's ability to circulate blood throughout the body becomes severely impaired. Another common cardiovascular issue among survivors is high blood pressure, often a result of chemotherapy and radiation therapy. The use of these therapies can cause endothelial damage (the cells lining blood vessels), leading to the stiffening of blood vessels and increased resistance to blood flow. Additionally, some survivors may develop secondary hypertension due to kidney damage, which is a known complication of cancer treatments. Survivors of neuroblastoma who received radiation therapy to the chest or abdomen are at increased risk of early-onset coronary artery disease (CAD). Radiation can damage the arteries, leading to the early buildup of plaque and narrowing of the vessels. CAD can subsequently lead to heart attacks, angina and other serious cardiovascular issues. Both chemotherapy and radiation treatments have been linked to an increased risk of arrhythmias—abnormal heart rhythms—among survivors. These irregular rhythms can range from minor palpitations to life-threatening arrhythmias, which can significantly impair quality of life and even be fatal [2].

Endocrine late effects are among the most common and significant long-term consequences faced by survivors of neuroblastoma. These effects

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are typically related to the treatments used, particularly surgery, radiation and chemotherapy. Survivors who received radiation therapy to the brain, particularly to the hypothalamic-pituitary region, are at risk for developing growth hormone deficiency. This can lead to stunted growth in childhood and in adulthood, it may result in fatigue, weakness and a reduced quality of life. The pituitary gland, responsible for secreting growth hormone, can also be affected by chemotherapy, leading to similar deficits. Radiation therapy to the neck or head area can affect the thyroid gland, leading to hypothyroidism (underactive thyroid) or hyperthyroidism (overactive thyroid). Hypothyroidism, the most common outcome, can cause fatigue, weight gain and developmental delays in children. On the other hand, hyperthyroidism can result in increased heart rate, weight loss and nervousness. Regular thyroid function tests are important for monitoring these risks in neuroblastoma survivors. Both male and female survivors of neuroblastoma are at risk for fertility issues due to the gonadotoxic effects of chemotherapy and radiation therapy. In females, ovarian failure and early menopause can occur, leading to difficulties in conceiving. Males may experience low sperm count or complete infertility due to damage to the testes. These fertility issues are particularly concerning for adolescent and adult survivors who may wish to have children in the future. The adrenal glands, which are responsible for producing critical hormones like cortisol, can be affected by neuroblastoma treatments. Survivors who underwent surgery to remove adrenal glands or radiation therapy to the area may develop adrenal insufficiency. This condition can cause fatigue, weakness, low blood pressure and a compromised ability to handle stress. Corticosteroid replacement therapy is often required to manage adrenal insufficiency [3].

Survivors who underwent intensive chemotherapy and radiation therapy, particularly to the brain or spinal cord, are at risk for developing cognitive impairments. These can include difficulties with attention, processing speed, memory and problem-solving abilities. The extent of cognitive impairment often correlates with the age at which the child received treatment, with younger children being more susceptible to brain damage. Many neuroblastoma survivors experience learning disabilities that may not become apparent until they are older and encounter more complex academic demands. These learning disabilities can manifest in challenges with reading, math, or other subjects requiring complex reasoning. Survivors may need special educational support to help them navigate their academic environment successfully. Executive functions refer to the higher-level cognitive processes that allow individuals to plan, make decisions, control impulses and regulate emotions. Neuroblastoma survivors may experience deficits in these areas, which can affect their ability to manage daily tasks, make decisions and regulate their behavior. These deficits can impact academic achievement, social relationships and employment prospects in adulthood. In addition to cognitive impairments, neuroblastoma survivors may experience social and emotional challenges. These can include difficulties in forming and maintaining relationships, social isolation, anxiety and depression. Survivors may struggle to integrate into peer groups due to the impact of their illness and treatment on their social skills and emotional regulation [4,5].

## Conclusion

While survival rates for neuroblastoma have improved considerably, the late effects experienced by survivors continue to be a significant area of concern. Cardiovascular, endocrine and neurocognitive late effects can have a profound impact on the lives of survivors, affecting their physical health, quality of life and emotional well-being. It is essential for healthcare

providers to recognize and monitor these late effects in neuroblastoma survivors, providing early interventions and support to manage and mitigate their impact. Ongoing research into the mechanisms behind these late effects and the development of strategies to prevent or minimize their occurrence is crucial for improving the long-term outcomes for neuroblastoma survivors. Advances in survivorship care, including personalized follow-up plans and multidisciplinary care teams, will be vital in supporting survivors as they transition into adulthood. While the fight against neuroblastoma has seen significant victories, the journey for survivors is far from over. A comprehensive approach to long-term care that addresses cardiovascular, endocrine and neurocognitive late effects is essential for ensuring that these young survivors can lead fulfilling lives after their cancer treatment has ended.

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## Acknowledgement

None.

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## Conflict of Interest

None.

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