CANCER SURVIVORS
SYMPOSIA SERIES
Issues & Solutions for Life After Cancer

Long-Term Effects of Cancer and its Treatment
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Executive Summary

Long-term Considerations After Chemotherapy and Stem Cell Transplantation
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A. Background Information—Stem Cell Transplantation
- First bone marrow transplant—1958.
- Many improvements and new knowledge about the treatment since.
- Two-types of Stem Cell Transplant
  a) Autologous
     --Patient serves as own donor—stem cells are taken out prior to high dose of chemotherapy and then infused back to rescue the bone marrow.
     --Allows for higher dose of chemotherapy .
  b) Allogeneic
     --Donor/recipient interaction—family, donor pool, umbilical cord blood are all donor sources.
     --High dose chemotherapy—donor cells strengthen the body's ability to fight the cancer.
- Stem cell transplants are used to fight numerous cancers and non-cancer diseases.
- More than 40,000 transplants are performed annually.

B. Long-term Complications of Chemotherapy/Bone Marrow Transplants
- Bone Loss
  a) Avascular necrosis is an injury that happens to certain bones because blood supply is compromised in that area.
  b) Associated with use of steroids
  c) Occurs most often in hips.
  d) Bone thinning occurs in 50-60% of patients, and may lead to diagnosis of osteoporosis in 20%.

e) Additional risk factors include family history, low testicular/ovarian function, use of G-CSF (Newpogen), kidney dysfunction.
f) Prevention: exercise, bisphosphonates, Calcium/Vitamin D, hormone replacement therapy.
g) Risk/benefit of hormone replacement therapy must by individually assessed.

C. Gonadal Dysfunction
- Therapy-related menopause is frequent.
- Can happen purposefully during treatment, but an also occur from certain high-dose chemotherapies or radiation.
- Absent menses, insufficient sperm production more often after radiation.
- Sexual dysfunction more often related to Graft versus Host Disease (GVHD).
- Testicular cancer survivors perceived less problems than those with normal controls.
- Sexual function impairment by hormonal changes can manifest as loss of lubrication, vaginal mucosal thinning, low testosterone levels associated with lower libido.
- There are interventions available, issues should be discussed.

D. Fertility After Chemotherapy
- Infertility is not a given and recovery does sometimes occur.
- No evidence that pregnancy after breast cancer compromises survival/relapse risk.
- Decision to have children more related to risk of recurrence—not physical ability.
- No evidence that children of breast cancer survivors have negative effects on mother's therapy.

E. Graft-Versus-Host-Disease (GVHD)
- Problem unique to allogeneic stem cell transplantation, when cells from another donor are used.
- Occurs when the immune therapy response attacks not just the malignancy but the normal organ functions, too.
- Has big impact on quality of life after transplantation.
- Occurs 30% of the time in family-member transplants.
- Occurs as much as 60-70% after a mismatch or unrelated transplant.
- Can present in many ways:
  a) Skin (sclerodermal-like, hair loss, nail changes)
  b) Mucous membranes (dry eyes/mouth, caries, vaginal dryness)
  c) Gastro-Intestinal (dry swallowing, cholestasis, malabsorption)
  d) Lung (bronchiolitis obliterans/accelerated emphysema)
  e) Immunity—defects in antibody production and cellular immunity
- May require prolonged therapy or immunosuppressants.

F. Pulmonary Risks
- GVHD can affect the lungs.
- Idiopathic Pneumonitis is an immune-mediated reduction in lung function similar to emphysema or chronic obstructive pulmonary disease.
- Chemotherapy can be associated with Pulmonary Fibrosis—5-10% in people with testicular cancer where bleomycin has been used.
- Can occur years after prolonged use of Carmustine for central nervous system tumors.
- Surgery in the lung area can lead to infections or thickening of the lining around the lung, leading to exercise intolerance.

G. Cardiac Risks
- Radiation to the chest (thoracic or breast) radiation can lead to myocardial infarction (increased risk of heart attack).
- Testicular cancer patients also have increased risk of MI from the use of Cisplatin and due to hormonal changes after orchiectomy.
- Can manifest as Metabolic Syndrome or insulin resistance (adult-onset diabetes)—this is treatable and reversible
- Some chemotherapies have some congestive heart failure risk.

H. Infection Risks:
- After transplant, it sometimes takes a while for immunity to come back to normal.
- Some agents lead to long-term reduction of immune system cells.
- Early infection problems usually related to mucositis and bacterial infections from neutropenia.
- Later issues may be more fungal, viral and encapsulated bacteria.
- For allogeneic transplants, may take up to two-years for immune system to recover, longer if patient has GVHD.
- It is very common for patients to have low immunoglobulins due to abnormal splenic functions.

I. Secondary Cancers:
- Post-transplant survivors are 4-11 times more likely to develop secondary cancers.
- Cumulative incidence of secondary cancers is 10-12% at 15 years after first diagnosis.
- Risks are related to:
    a) Intensive chemotherapy
    b) Previous chemotherapy and/or radiation
    c) Immunosuppression in allogeneic transplants
    d) Infections
        --Epstein Barr Virus leads to risk of lymphoma
        --HPV—related to cervical cancer
        --Hepatitis C Virus—related to hepatitis and hepatoma

- 4-8% incidence of AML/Myelodysplasia usually within 12-14-month time period after treatment. Risk related to:
    a) Treatment with Alkylators, topoisomerase inhibitors, radiation therapy
    b) Stem cell transplant with less than I million stem cells
    c) Total body radiation
- Solid Tumors—cumulative incidence is 6-11% at 15 years
    a) Skin cancer, breast cancer, oral cancers
    b) Highest risk is in transplant patients under age 10
    c) Related to immunosuppression, radiation, GVHD, viral reactivation.

J. Quality of Life, Post-Bone Marrow Transplant
- Physical functioning returns to pre-BMT levels by one year
- 85% of transplant patients return to work or school.
- At one year, there was a modest decline in IQ of 6 points, but no changes by 1-3 years.
- Highest risk is to children under age 6, and especially those under age 3 at time of treatment.
- Majority of survivors have good psychological health.
    a) 35% show high levels of anxiety
    b) 60% felt vulnerable
    c) 35% showed unfulfilled needs in their love lives
- No difference in family/peer relationships, school performance, self-esteem.

K. Comparative Work Ability
- Results of a study of 591 patients showed no difference in work ability of cancer survivors.
- Physical limitations to work occurred in 26% after treatment
- Cognitive limitations occurred in 19%, more common after chemotherapy.
- Work limitations least likely when patients have a strong commitment to work and a good social climate at work.

L. Family Stressors
- Sibling donors can feel responsible for complications.
- Anniversaries of diagnosis or start/end of treatment can be difficult for all family members.
- Younger parents with unresolved anxiety or depression at the time their child or they go through transplant require intervention because they have higher incidence of post-traumatic stress disorder.

M. Long-Term Follow-up

Problem	***Cause***	***Therapy***	***Monitoring***
ORAL Lichen planus Sicca	cGVHD	Immunosuppressants Topical Lubricants Pilocarpine Flouride Rinses	Exams at least every 6 months to reduce secondary cancer risk
EYES Sicca Cataracts	cGVHD Radiation	Immunosuppressants Lacrimal Duct Occlusion	Biannual Exams (more frequent corneal injury)
SECONDARY CANCERS	Immune-suppression Radiation cGVHD	Disease-specific Therapy	Annual Physical PAP Smears Blood Testing Mammography Fecal Occult Sun Exposure Avoidance
HEART Atherosclerosis	Chest Radiation High Lipids Hypertension	Control blood pressure Lipid lowering therapy	Lipid profile monitoring Annual physical exam Exercise testing if needed
LUNG Bronchiolitis Obliterans Bronchiectasis	cGVHD hypogammaglobulins	Immunosuppressants Prophylactic antibiotics IgG replacement	PFTs at least every 6 months
LIVER Cholestasis Viral Hepatitis Iron overload	Immunesuppression cGVHD Transfusions	Immunosuppressants Antiviral therapy Iron chelation therapy	Annual LFT Liver biopsy if needed Periodic viral testing Baseline Ferritin
KIDNEY Azotemia	Hypertension Medications	Control blood pressure Monitor medication levels	Annual monitoring
ENDOCRINE Thyroid Ovary Testes Bone	Radiation Steroids Inactivity	Hormone replacement Bisphosphates Calcium/Vitamin D Exercise	-Annual thyroid function -Annual gonadal hormone testing if delay -Evaluation by endocrine for growth delay -Bone mineral testing -Monitoring for secondary cancer