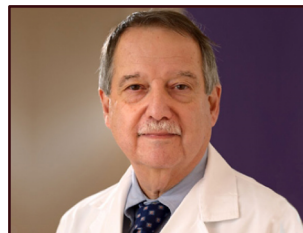




Late Effects after a Pediatric Transplant, Transitioning to Adult Care

Celebrating a Second Chance at Life
Survivorship Symposium

April 30 - May 6, 2022



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Continuous Care for Pediatric Patients After Transplantation

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Goals for Pediatric Transplant Patients in the Long-Term Survivorship Clinic

- Prevent complications
- Provide effective treatment for complications that cannot be prevented
- Promote lifelong healthy habits
- Support measures that improve quality of life
 - School
 - Occupation/vocation
 - Interpersonal/social
 - Emotional

Recognize Your Specific Circumstance

- Illness which necessitated transplant
 - Diagnosis impacts long term concerns
- Side effects of pre-transplant treatment
- Specifics of transplant therapy
 - Conditioning
 - GVHD preventive therapy
 - Complications

Long Term Survivorship Recommendations

- Be the Match (National Marrow Donor Program)
 - bethematch.org/patients-and-families/life-after-transplant/
- International Late Effects of Childhood Cancer Guideline Harmonization Group
 - ighg.org/guidelines
- Children's Oncology Group
 - survivorshipguidelines.org

Re-Immunization

- Begin by 12 months:
 - DTaP, Pneumococcus, Hemophilus, Meningococcus, Hepatitis A/B, Polio
 - Inactivated virus vaccine
- No sooner than 24 months and no GVHD or immunosuppression:
 - Measles, Mumps, Rubella, HPV
 - *if no antibody, Varicella vaccine (not Shingles vaccine)
- SARS CoV2 and Influenza

Genetic Conditions and Late Effects

- Non-bone marrow manifestations of genetic diseases
 - Fanconi Aplastic Anemia
 - Dyskeratosis Congenita
 - Blackfan-Diamond
 - Schwachman-Diamond
 - Sickle Cell Anemia and Thalassemia
 - Immunodeficiency Disorders
 - Genetic disorders of metabolism

Oral Care

- Up to half of children undergoing transplantation will develop oral complications
- Conditioning therapy and age at diagnosis
 - Cavities (caries)
 - Dry mouth
 - Tooth development
- Orthodontia and routine dental care

Heart Health – Potential Problems

- Over a lifetime patients are at risk of cardiac complications
 - Cardiomyopathy with/without heart failure
 - Pericarditis
 - Valvular heart disease
 - Coronary heart disease
 - Cardiac arrhythmia

Heart Health – Risk Factors

- Anthracyclines total dose
 - Doxorubicin equivalent dose:
 - daunomycin, doxorubicin, idarubicin, epirubicin, amsacrine
- Irradiation dose
 - TBI
 - Chest radiation
- Combined or separate administration
- Other factors contribute to risk
 - Smoking, obesity, diabetes, dyslipemia, sedentary lifestyle, etc.

Heart Care Screening Recommendations*

- Risk-based: dose radiotherapy and/or anthracyclines
- High risk, lifetime risk for cardiac disease 36%
 - Echocardiogram every 2 years
- Intermediate risk
 - Echocardiogram every 5 years
- Low risk
 - Echocardiogram not necessary

*International Late Effects of Childhood Cancer Guideline Harmonization Group

Bone Health

- Osteochondroma (exostosis)
 - TBI
 - Benign tumor at metaphyseal sites (growth plates)
- Avascular necrosis
 - Hip most frequent
 - MRI preferred imaging technique

Bone Health

- Osteoporosis
 - TBI, cranial or craniospinal radiotherapy, steroid
 - Hypogonadism and growth hormone deficiency
 - Bone fragility can lead to non-traumatic fractures
- DXA scan
- Calcium and vitamin D
 - No smoking, moderate alcohol, and physical activity
 - Bisphosphonate

Kidney Health – Risk Factors

- Kidney function often diminished without signs or symptoms
 - Chemotherapy:
 - ifosfamide, cisplatin, methotrexate
 - Radiotherapy (RT)
 - Other drugs:
 - tacrolimus, cyclosporin, vancomycin, foscarnet, etc.

Kidney Health – Monitoring, Prevention

- Monitor Kidney Function
 - Urinalysis
 - Creatinine Clearance or Glomerular Filtration Rate
- Hypertension
- Avoid NSAIDs: I
 - buprofen, naprosyn, etc.
- Nephrologist for hypertension or proteinuria

Lung Health

- Lung disease associated with GVHD or early post transplant lung injury
 - Bronchiolitis obliterans (BOS)
 - Cryptogenic organizing pneumonia (BOOP)
- Lung injury
 - Drugs: bleomycin, busulfan, nitrosureas
 - Radiotherapy (RT): TBI, chest RT

Lung Health – Monitoring, Prevention

- Pulmonary function test
 - Pretransplant
 - Diffusion capacity
 - 6 years
 - Repeat during first 12 months post-transplant
- **NO SMOKING EVER**
 - Second-hand smoking

Skin Health

- Chronic GVHD
 - Loss of pigmentation, ulcers, thickened skin, eczema-like rash
- Malignancy
 - Radiation therapy and cGVHD
 - Sun exposure
 - Melanoma, squamous cell carcinoma, and basal cell carcinoma
 - Mole check

Pituitary Gland Health

- Pituitary Gland
 - Growth hormone deficiency
 - Gonadotrophic hormone deficiency
 - FSH
 - LH
 - Adrenocorticotrophic hormone deficiency (ACTH)
 - Thyroid stimulating hormone deficiency (TSH)
- Radiation (TBI)
- Disease: leukemia, brain tumor, other

Pituitary Gland Health - Interventions

- Growth hormone deficiency
 - Insulin Growth Factor (IGF) and IGF Binding Protein
 - Growth in height over time
 - Bone age
- Thyroid and gonad function can impact growth
- Growth hormone therapy before puberty
 - Precocious puberty

Thyroid Gland Health – Potential Problems

- Thyroid
 - Hypothyroidism
 - TBI or RT to neck: mantle irradiation, mediastinum
 - TSH and FT4
 - Hyperthyroidism
 - Thyroid cancer
 - Neck exam and palpation
 - Ultrasound

Male Health – Puberty, Fertility

- Testes
 - TBI or Radiation Therapy
 - Alkylating agents or platinum-based
 - Pituitary
- Before or after puberty
 - Delayed or arrested puberty
 - Post pubertal gonadal deficiency
- Infertility

Male Health – Potential Interventions

- Testis
 - Germ cells (Sperm cells)
 - FSH (follicle stimulating hormone)
 - Pubertal development and masculinity (Leydig cells)
 - LH (luteinizing hormone)
 - Testosterone
 - Before puberty (12 years)
 - Morning testosterone, LH and FSH
 - Sperm cryopreservation

Female Health – Puberty, Fertility

- Ovary
 - Estrogen and germ cell development
 - FSH and LH complementary
 - Germ cells are fixed at birth
 - Puberty and fertility dependent upon total germ cell number
 - Failure to feminize
 - Infertility

Female Health – Ovarian Failure

- Primary or Secondary Ovarian Failure
 - Before puberty
 - Failure to initiate or complete puberty
 - Post puberty
 - Failure to resume menses
 - Premature menopause
- Menopausal

Reproductive Health

- Infertility rate 75%
 - Age at treatment
 - Prepubertal male
 - Postpubertal female
- TBI
- Busulfan
- Pregnancy outcome
 - Miscarriage and other complications, BUT
 - Healthy babies

Eye and Ear Health

- Neurocognitive Development
 - Speech
 - Behavior
 - Schooling
- Hearing loss and tinnitus
 - Cisplatinum (platinum-derivatives)
 - Brain radiotherapy (RT)
 - Ventricular shunt
 - Genetic disorders
- Cataract formation; corneal opacification
 - RT
 - Genetic disorders
- CMV retinitis

Hepatic (Liver) Health

- Liver injury
 - Drugs, Radiation Therapy, veno-occlusive disease, viral infection
 - Transfusion iron overload
 - 10 red blood cell transfusions
- Liver enzymes, ferritin, MRI
- Focal nodular hyperplasia (FNH)
- Nonalcoholic fatty liver disease
 - Nonalcoholic steatohepatitis (NASH)

Metabolic Syndrome

- Constellation
 - Hypertension
 - Abdominal Obesity (waist circumference)
 - Hyperlipidemia
 - Abnormal glucose metabolism
- Cardiac disease
- Diabetes

Metabolic Syndrome – Cause, Prevention

- Causes
 - Uncertain but radiation therapy and drugs must be suspect
 - Growth hormone insufficiency
 - Steroids – dose and duration
- Obesity
 - Inflammatory state
- Diet, weight control, and physical activity

Malignancy (cancer)

- Incidence remains uncertain
 - Overall, twice general population
 - Risk increases over time
 - Both autologous and allogeneic stem cell transplant
 - MDS/AML
 - Lymphoproliferative disease
 - Breast cancer

Malignancy – Causes after Transplant

- Multiple variables
 - Patient specific
 - genetic factors
 - age at transplant
 - Diagnosis
 - Conditioning therapy
 - Radiation therapy
 - GVHD

Malignancy – Screening, Prevention

- Breast cancer
 - Hodgkin lymphoma
 - Thyroid cancer
 - Annual MRI and breast US or mammogram begin 25 years or 8 years post treatment
- Skin squamous cell carcinoma
 - Chronic GVHD
- CNS tumor
 - CNS leukemia and cranial RT

Neurocognitive Development

- Neurocognition:
 - brain function that generate complex behaviors of day-to-day life
- Many variables can impact neurocognition
 - TBI and cranial irradiation
 - Transplant at young age
- Most patients test within the average population range

Neurocognitive Development

- Neurocognitive testing by first anniversary
 - Ideal, test before conditioning
 - Repeat testing as needed but at a minimum at new stage of education: preschool, first grade, 6th grade, etc.
- Memory, concentration, organization
- Timely and appropriate intervention

Fatigue

- “the persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion that is not proportional to recent activity and interferes with usual functioning”
- Daytime sleepiness
- Poor social, behavioral, adaptive functioning
- Active interventions have shown benefit

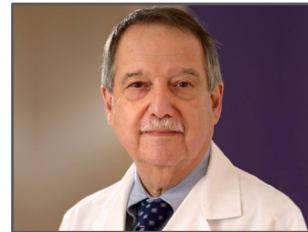
Exercise Tolerance

- Integration: cardiac, pulmonary, muscular systems
- Exercise intolerance
 - Global longitudinal strain vs. ejection fraction
 - Oxygen uptake
 - Heart rate response

Final Thoughts

- Create a mindset, lifelong!
- Establish post transplant follow up
 - Transplant center programs
 - Knowledgeable providers
- Life-style health habits
 - Diet
 - Exercise
 - Address unhealthy behavior: obesity, smoking, drugs, alcohol, anxiety, depression
- Healthy habits are essential to promote healthy adults

Questions?



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