Survivorship Care

Approaching late effects in adolescent and young adult patients

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What is the fuss about?

Most adult survivors of childhood cancer are not followed up on a regular basis.

Recent data from NIH Children’s Cancer Study shows 51% of 14,000 respondents had not been seen in the last 2 years.

Late effects are a real and common issue in these patients.
Grading of late effects in Young adult Cancer survivors in Ambulatory Adult Setting

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N = 96, Single Institute, Dx 1973-1995
Grading of late effects in Young adult Cancer survivors in Ambulatory Adult Setting

<table>
<thead>
<tr>
<th>Cancer</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukemia</td>
<td>32</td>
</tr>
<tr>
<td>Acute lymphoblastic leukemia</td>
<td>28</td>
</tr>
<tr>
<td>Acute myelogenous leukemia</td>
<td>4</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>23</td>
</tr>
<tr>
<td>Osteosarcoma</td>
<td>9</td>
</tr>
<tr>
<td>Rhabdomyosarcoma</td>
<td>6</td>
</tr>
<tr>
<td>Other sarcomas</td>
<td>8</td>
</tr>
<tr>
<td>NHL/HD</td>
<td>25</td>
</tr>
<tr>
<td>NHL</td>
<td>11</td>
</tr>
<tr>
<td>HD</td>
<td>14</td>
</tr>
<tr>
<td>Wilms’ tumor</td>
<td>9</td>
</tr>
<tr>
<td>Other</td>
<td>7</td>
</tr>
<tr>
<td>Neuroblastoma</td>
<td>3</td>
</tr>
<tr>
<td>Langerhans’ cell histiocytosis</td>
<td>2</td>
</tr>
<tr>
<td>Hemangiosarcoma</td>
<td>1</td>
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</table>
Grading of late effects in Young adult Cancer survivors in Ambulatory Adult Setting

<table>
<thead>
<tr>
<th>Late Effects Graded as per CTCv2</th>
<th>Percent</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No CTCv2 late effect</td>
<td>31%</td>
<td>30/96</td>
</tr>
<tr>
<td>Late effect</td>
<td>69%</td>
<td>66/96</td>
</tr>
<tr>
<td>Single late effect</td>
<td>33%</td>
<td>32/96</td>
</tr>
<tr>
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- Long term physiological / psychological burden
- Life threatening toxicities
How to assess a patient for late-effects
• 20% of cancer survivors exposed to anthracyclines are at risk of developing cardiovascular complications (cardiomyopathy) with 7% at risk of congestive heart failure many years following therapy.

• It is important that patients are aware of any treatments they have received that may affect the heart

**Anthracyclines**

- Doxorubicin (Adriamycin®)
- Daunorubicin/daunomycin (Cerubidine®)
- Idarubicin (Idamycin®)
- Mitoxantrone (Novantrone®)
- Epirubicin
Heart problems can also result from radiotherapy to the:

- Chest or thorax (including mantle, mediastinal, and axillary treatment fields)
- Spine (chest or “thoracic” portion)
- Abdomen
- Total body irradiation (TBI)

Cardiovascular side effects can include:

- Left ventricular dysfunction / cardiomyopathy
- Arrhythmia (scarring)
- Valvular stenosis or insufficiency
- Coronary artery disease
## Schedule for Echocardiogram or MUGA Scans

<table>
<thead>
<tr>
<th>Age at treatment*</th>
<th>Chest radiation</th>
<th>Total anthracycline dose**</th>
<th>Recommended frequency of ECHO or MUGA***</th>
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<tbody>
<tr>
<td>&lt; 1 year</td>
<td>Yes</td>
<td>Any</td>
<td>Every year</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>&lt; 200 mg/m²</td>
<td>Every 2 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥ 200 mg/m²</td>
<td>Every year</td>
</tr>
<tr>
<td>1 to 4 years old</td>
<td>Yes</td>
<td>Any</td>
<td>Every year</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt; 100 mg/m²</td>
<td>Every 5 years</td>
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<td></td>
<td>No</td>
<td>≥ 100 to &lt; 300 mg/m²</td>
<td>Every 2 years</td>
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<td></td>
<td></td>
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*age at first treatment with anthracycline or chest radiation (whichever was given first)

**based on total doses of doxorubicin/daunorubicin or the equivalent doses of other anthracyclines

***MUGA scans may be used for patients who received anthracycline chemotherapy without radiation; 
Echocardiograms are the preferred test for those who received radiation involving the heart because the test provides more detailed information regarding structural damage, including valve structure.
Keeping your heart health after treatment for childhood cancer

When to refer to Cardiology

- Any abnormal findings on surveillance
- Stress test advisable 5–10 years after therapy if received
  - > 40 Gy to heart alone OR
  - 30 Gy & anthracycline
- Female survivors who have
  - received anthracycline, chest irradiation or high dose cyclophosphamide &
  - are pregnant

Additional Patient information

- No smoking, Healthy body weight, Exercise 30 mins most days
- Monitor for CVS risk factors (lipid profile, HbA1c, fasting glucose) every 2 years
Several Therapeutic approaches cause damage to the lungs

- Bleomycin (See the “Bleomycin Alert” Health Link for more information)
- Carmustine (also known as BCNU)
- Lomustine (also known as CCNU)
- Busulfan
- Radiation to the chest
- Total body irradiation (TBI)
- Surgery to the chest or lung (this does NOT include surgery for placement of a central line, such as a Hickman, Broviac, Port-a-Cath or Mediport)
- Bone marrow transplant or stem cell transplant from a donor other than yourself (allogeneic transplant), if you then developed chronic graft-versus-host disease (chronic GVHD)
What problems can develop?
- Pulmonary fibrosis
- Bronchiectasis / recurrent pneumonia
- Inflammation of lung small airways (bronchiolitis obliterans)
- Restrictive or obstructive lung disease

What monitoring is recommended?
- Yearly review
- Lung function tests up to 2 years after therapy (3 monthly after BMT)

Special Precautions for at-risk patients
- Pneumococcal vaccine (post therapy) and yearly influenza vaccine
- Avoid smoking
- Avoid scuba diving until full workup complete
What problems can develop?
Certain chemotherapy, radiation therapy and surgery can affect female reproduction.

Alkylator doses are important - > 4 gm/m² some degree of damage, 
> 8gm/m² definite infertility

Radiation can affect fertility either directly (primary – RThx to ovaries) or secondary (RThx to brain decreased LH/FSH)

Surgery – if both ovaries removed early menopause 
if one ovary premature menopause can result
Female Reproductive Issues post therapy

Risk Factors

- **Radiation therapy** to any of the following areas:
  - Whole abdomen
  - Pelvis
  - Lower spine (lumbar and sacral areas)
  - Total body (TBI)
  - Head/brain (cranial)—if dose was 30 Gy (3000 cGy/rads) or higher
Female Reproductive Issues post therapy

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- **Alkylating agents:**
  - Busulfan
  - Carmustine (BCNU)
  - Chlorambucil
  - Cyclophosphamide (Cytoxan®)
  - Ifosfamide
  - Lomustine (CCNU)
  - Mechlorethamine (nitrogen mustard)
  - Melphalan
  - Procarbazine
  - Thiotepa

- **Heavy metals:**
  - Carboplatin
  - Cisplatin
Female Reproductive Issues post therapy

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- **Non-classical alkylators:**
  - Dacarbazine (DTIC)
  - Temozolomide

- **Surgery:**
  - Removal of one or both ovaries
Female Reproductive Issues post therapy

What are the effects on the reproductive system?
- Failure to enter puberty
- Temporary cessation of menstrual cycles
- Permanent cessation of menstrual cycles (premature menopause)
- Oestrogen deficiency
- Infertility
- Pregnancy risks (TBI, anthracycline)

What monitoring is recommended?
- Yearly review with LH, FSH, oestradiol if any abnormalities should be referred to endocrinologist for review
- For patients with ovarian failure bone density should be assessed
- If patient is at risk of premature ovarian failure consider referral to IVF specialist
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Male Reproductive Issues post therapy

What are the effects on the reproductive system?

Infertility and/or testosterone deficiency (Leydig cell failure) are the main consequences of cancer therapy for the young.

Testosterone important for
- Commencing puberty
- Maintain muscular development
- Maintain muscular and bone strength
- Proper distribution body fat
- Sex drive and ability to maintain erection
- Energy levels
Male Reproductive Issues post therapy

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- **Surgeries that may cause infertility or disrupt normal sexual functioning include**
  - Removal of both testicles (this surgery will always result in infertility)
  - Retroperitoneal lymph node dissection (RPLD)
  - Removal of tumor in the retroperitoneal area
  - Cystectomy (removal of the bladder)
  - Prostatectomy (removal of the prostate)

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- Carboplatin
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What monitoring is recommended?

- Yearly check up with LH/FSH +/- Testosterone
- Males treated < 1 year should have endocrine follow up from 11 years of age
- Any abnormal results should result in a referral to endocrinologist
- Leydig cell failure can be treated with testosterone (patches, IM, topical gel)
- Perform semen analysis when warranted (i.e. wanting to start family)
- Advise use of contraception as recovery of sperm function may occur months or years down the track!
Secondary Malignancy risk

These include

Breast Cancer
Colorectal cancer
Leukaemia (AML M5)
Sarcoma
Skin Cancer

Reducing the risk of secondary cancers
Any patient treated with radiation to the chest is at risk with the precise risk relating to dose and technique.

Other risk factors for BC that apply to all women:
- Early menstruation (< 12) or late menopause (>55)
- Never having a baby or first baby after age 30
- Family history of breast cancer
- Being overweight and/or inactive

Timing of Breast Cancer
- 5-9 years following radiation therapy
Breast Cancer Risk

Management (For patients with > 20 Gy irradiation to chest)
- Encourage patients to do monthly breast examination and report changes to health care provider immediately
- Yearly breast examination by health care provider yearly until 25 years of age, then every 6 months
- Yearly mammogram and breast MRI from age of 25 years or 8 years after received irradiation (whichever comes last).

For lower doses of chest irradiation or TBI
Guidance is not as strict
However, probably warrants early follow up
Skin Cancer after Childhood Cancer

Who is at risk
Any patient with radiation to the skin including Total Body Irradiation (TBI)
Survivors with graft-versus-host-disease following allogenic BMT

What problems can occur
Telangiectasia
Fibrosis
Scleroderma
Vitiligo
Pigmentation (bleomycin, busulphan, cyclophosphamide, actinomycin-d, 5-FU, hydroxyurea and methotrexate)
Skin cancers
Skin Cancer after Childhood Cancer

Skin Cancers

Basal Cell Carcinoma
- Most frequently seen
- Surgical excision
- Protect against BCC by judicious sun protection

Squamous Cell Carcinoma
- Associated with radiation exposure and long-term antifungal use (voriconazole)
- Protect against SCC by judicious sun protection

Melanoma

Recommended monitoring
- Yearly reviews with general practitioner with interest in skin OR dermatologist.
- Clinical review with treating clinician 6 monthly
Reducing the risk of secondary malignancy

Anxiety provoking for all patients
Risk varies, usually 2-4%

Leukaemia
Usually AML, poor prognosis
Related to alkylators (cyclophosphamide, nitrogen mustard), epidophyllotoxins (etoposide, teniposide), anthracyclines (doxorubicin, daunorubicin) or transplant recipients (auto/allo)
Usually within the first 10 years since therapy completion

Solid tumours
Usually relate to radiation exposure
Include skin cancer, breast cancer, CNS tumours, thyroid cancer, bone tumours
Usually > 10 years after therapy completed
Reducing the risk of secondary malignancy

Familial cancer syndromes
- Affect < 10% of patients
- Clear history of relatives developing cancer < 50 years of age
- Usually related to p53 defects (Li Fraumeni Syndrome)

Monitoring recommendations
- Yearly check-up with competent health care provider
- Full blood count (as indicated) in first 10 years for leukaemia risk patients
- Appropriate screening for radiation fields (i.e. breast mammograms)
Reducing the risk of secondary malignancy

Monitoring recommendations

Educate our patients

- Look out for easy bruising, excessive fatigue, bone pain, changes in moles, sores that do not heal, lumps or bumps, difficulty swallowing, changes in bowel habits, persistent abdominal pain, changes in stools, persistent cough or hoarseness, shortness of breath, bloody sputum, discolouration or sores in the mouth, persistent headaches, vision changes, early morning vomiting.

Avoid cancer promoting behaviours

- No smoking
- SPF protection
- Moderate alcohol intake and health diet
- Vaccinate (esp. Hep B and HPV)
Cataracts are not an uncommon risk after therapy.

Causative agents:
- Busulphan
- Cortico-steroids (i.e. dexamethasone, prednisolone)

Radiation therapy:
- To eye and orbits
- Cranial (head/brain)
- Total Body Irradiation

Risk for cataracts increases with:
- Higher doses
- Time
Eye Health – Cataracts

Recommended monitoring
Eye evaluation at yearly check up

Opthalmology review **yearly**
TBI
High dose radiation (> 30 gy) to head, orbits, eyes
A tumour involving the eye

Opthalmology review **3 yearly**
Lower doses radiation
Chemotherapy exposure
Eye Health – Cataracts

Recommended monitoring
Eye evaluation at yearly check up

Opthalmology review yearly
- TBI
  High dose radiation (> 30 gy) to head, orbits, eyes
  A tumour involving the eye

Opthalmology review 3 yearly
- Lower doses radiation
- Chemotherapy exposure
Osteonecrosis

Typically referred to as AVN, ‘aseptic necrosis’ or ‘ischaemic bone necrosis’

Results from temporary or permanent lack of blood supply to the bones

Typically effects the ends of long bones (epiphysis) – femur, upper arms/shoulder, ankle

Risk factors

Corticosteroids (dexamethasone, prednisolone)

Symptoms

Can be asymptomatic OR have pain in the joint
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Osteonecrosis

**Monitoring recommendations**
Screen using MRI or plain XR if symptoms arise.
Most patients will have been screened at end of therapy if high-dose steroids throughout.

**Treatment**
Dependent on persons age, stage of disease, location and amount of bone involved, status of cancer treatment
Referral to orthopaedics should be made
Manage pain according to need
Reduce weight bearing exercises and modify activity in consultation with physiotherapy/ orthopaedics
Keeping bones healthy after cancer

Important to educate our patients to the risk of osteoporosis

Risk factors related to cancer therapy include
- Corticosteroid exposure
- Methotrexate
- Radiation to weight bearing bones
- Hormonal insufficiency
- Graft-vs-host disease with steroids used as a consequence to control disease
- Prolonged periods of inactivity
- Additional medication risk factors – certain anti-convulsants, high doses heparin
Maintaining healthy bones

- Weight bearing exercise
- 1000-1500mg calcium per day, 400 units vitamin D daily

Recommended Monitoring

For those patients at risk a baseline bone mineral density is recommended when they enter long-term follow up (2 years since therapy completed)

If poor bone health identified follow up scans may be recommended and should be discussed with endocrinology (? Bisphosphonate use)
Emotions / Mental Health after cancer

Diagnosis and Treatment

• Scary time with many uncertainties
• Need for multiple tests and procedures
• Anxiety at crucial timepoints (i.e. waiting for results)
• Missed opportunities school, work, socialisation
• Siblings often forgotten and have considerable anxiety which can be unaddressed
• Mixed emotions (angry, sad, scared, lonely, afraid) from all family members (patient, parents, siblings, friends)
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Emotions / Mental Health after cancer

After treatment

• Can bring new feelings
• Tend to switch from ‘here and now’ thinking to ‘long-term’, late effects, and start processing what they have been through.
• Range of feelings that are unique to each person
• Routine testing for late effects or even just talking about late effects can cause considerable stress
• Diagnosis of a late effect or side-effects related to therapy can open up many psychological scars
• Anniversaries around cancer events (diagnosis, end of treatment) or life changes (i.e. starting school, normalisation of social situations again) can bring a range of feelings including relief, happiness, sadness (loss of normal young life) and guilt (if they survived but others didn’t)
• Some young people think they are ’invincible’ as they have survived cancer which can lead to increased risk taking behaviours (drugs, reckless driving, poor studies etc.)
Emotions / Mental Health after cancer

What to expect

• Many survivors respond well and adapt to the stressors of this period
• Some survivors or their families may have periods of high anxiety and intense emotions that need medical intervention. These may include
  • Unwanted recall of unpleasant experiences during or after treatment
  • Physical or emotional overreactions
  • Going out of their way to avoid reminders of cancer
  • Frank depression / anxiety

Risk Factors
Female gender
Adolescent or Young adult age range at diagnosis
Prior trauma
Mental health problems prior to diagnosis or family history of
Low levels of social support
Cancer of CNS
Cancer treatment to CNS (i.e. whole brain irradiation)
Stem cell transplant
Emotions / Mental Health after cancer

Monitoring

• Assess emotional and social situation at yearly review with either GP or specialist
• Educate patients about when to seek help (i.e. changes in appetite, crying easily, social isolation, sleeping little or too much, feeling hopeless, increased irritability, feeling fearful, unwanted recall of unpleasant events)
• Refer on as necessary to psychologist (Treat Unique) or locally and use additional supports in the community (i.e. Canteen)
• Use Mental health plan to save costs
Tailored export support for adolescents and young adults living with cancer

- **Director** - Dr Rachel Conyers 0402 841 218
- **Clinical Nurse Co-ordinator** - Donna Gairns
- **Social Worker** - Christina Portelli
- **Pilates Instructor** - Rachael Fraser