# Symptom Management Guidelines:
## CANCER – RELATED FATIGUE AND ANEMIA

### Definition

**Cancer – Related Fatigue (CRF):** A subjective feeling of physical, emotional and/or cognitive tiredness; is often not relieved by rest.

### Contributing Factors

<table>
<thead>
<tr>
<th>Cancer Related &amp; Cancer Treatment Related</th>
<th>*Extent of disease may affect level of fatigue</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Chemotherapy (especially high dose chemotherapy followed by a blood or marrow transplant)</em></td>
<td><em>Radiation therapy</em></td>
</tr>
<tr>
<td><em>Surgery</em></td>
<td><em>Biotherapy (especially high dose interferon)</em></td>
</tr>
<tr>
<td><em>Inflammatory cytokines</em></td>
<td><em>Immunotherapy – Checkpoint inhibitors</em></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Relevant Medical History</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Fever and/or infection</em></td>
<td><em>Anemia</em></td>
</tr>
<tr>
<td><em>Hypothyroidism</em></td>
<td><em>Diabetes mellitus</em></td>
</tr>
<tr>
<td><em>Electrolyte disturbances (Sodium, Potassium, Calcium, Magnesium)</em></td>
<td><em>Cardiopulmonary, hepatic or renal dysfunction</em></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medications</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Opioids</em></td>
<td><em>Antidepressants</em></td>
</tr>
<tr>
<td><em>Antihistamines</em></td>
<td><em>Beta blockers</em></td>
</tr>
<tr>
<td><em>Phenytoin and other anticonvulsants</em></td>
<td><em>Benzodiazepines</em></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Advanced age</em></td>
<td><em>Life stressors, depression &amp; anxiety</em></td>
</tr>
<tr>
<td><em>Sleep/wake disturbance</em></td>
<td><em>Pain</em></td>
</tr>
<tr>
<td><em>Decreased activity, bed rest, deconditioning</em></td>
<td><em>Nutritional deficits, malnutrition and dehydration</em></td>
</tr>
<tr>
<td><em>Alcohol/substance abuse</em></td>
<td></td>
</tr>
</tbody>
</table>

### Consequences

- Chemotherapy dose delays, reductions, discontinuation of treatment
- Quality of life – distress, compromised role function and cognition, decreased functional status, exacerbation of other symptoms

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## Focused Health Assessment

<table>
<thead>
<tr>
<th>GENERAL ASSESSMENT</th>
<th>SYMPTOM ASSESSMENT</th>
<th>PHYSICAL ASSESSMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Contact and General Information</strong></td>
<td><strong>Normal</strong></td>
<td><strong>Vital Signs</strong></td>
</tr>
<tr>
<td>• Physician name - oncologist, family physician</td>
<td>• What is your normal energy/activity level/exercise?</td>
<td>• Frequency – as clinically indicated</td>
</tr>
<tr>
<td>• Pharmacy</td>
<td><strong>Onset</strong></td>
<td><strong>Observe for:</strong></td>
</tr>
<tr>
<td>• Home health care</td>
<td>• When did the fatigue begin? Is it related to a change in cancer treatment?</td>
<td>• Pallor</td>
</tr>
<tr>
<td>• Other healthcare providers</td>
<td><strong>Provoking / Palliating</strong></td>
<td>• Blood loss</td>
</tr>
<tr>
<td>• Allergies</td>
<td>• What brings on the fatigue?</td>
<td>• Labored breathing</td>
</tr>
<tr>
<td><strong>Consider Contributing Factors</strong></td>
<td>• Is there anything that makes the fatigue better?</td>
<td>• Poor capillary refill</td>
</tr>
<tr>
<td>• Cancer diagnosis</td>
<td>• Worse?</td>
<td>• Poor posture</td>
</tr>
<tr>
<td>• Cancer treatment(s) – note type and date of last treatment(s), concurrent treatments</td>
<td>• When do you feel the most tired?</td>
<td>• Cachexia</td>
</tr>
<tr>
<td>• Medical history</td>
<td><strong>Quality</strong></td>
<td>• Altered mobility, gait</td>
</tr>
<tr>
<td>• Medication profile</td>
<td>• What does it feel like?</td>
<td>• Peripheral edema</td>
</tr>
<tr>
<td>• Recent lab or diagnostic reports (e.g. CBC, electrolyte)</td>
<td>• Explore whether symptoms reflect drowsiness versus physical fatigue or mental versus physical fatigue</td>
<td>• Cognitive impairment</td>
</tr>
<tr>
<td>• Nutritional deficits or dehydration</td>
<td><strong>Region/ Radiation-N/A</strong></td>
<td>• Chest pain</td>
</tr>
<tr>
<td>• Decreased activity, bed rest and deconditioning</td>
<td><strong>Severity / Other Symptoms</strong></td>
<td><strong>Weight</strong></td>
</tr>
<tr>
<td>• Depression and anxiety</td>
<td>• Since your last visit, how would you rate your fatigue between 0-10? What is it now? At worst? At best? On average?</td>
<td>• Take current weight and compare to pre – treatment or last recorded weight</td>
</tr>
<tr>
<td>• Pain</td>
<td>• Do you have any other accompanying symptoms such as shortness of breath at rest or with activity, rapid heart rate, chest pain or leg heaviness?</td>
<td><strong>Treatment</strong></td>
</tr>
<tr>
<td>• Anemia</td>
<td><strong>Understanding / Impact on You</strong></td>
<td><strong>What medications or treatments are you using or have you used in the past? How effective are they? Any side effects?</strong></td>
</tr>
<tr>
<td>• Fever and/or infection</td>
<td>• Is fatigue affecting your mood? Anxiety, sadness, feeling stressed?</td>
<td>• Have you had a blood transfusion? When?</td>
</tr>
<tr>
<td>• Sleep / wake disturbance</td>
<td>• How much are you able to do in a day?</td>
<td>• When was your last cancer treatment?</td>
</tr>
</tbody>
</table>

### Vital Signs
- Frequency – as clinically indicated

### Observe for:
- Pallor
- Blood loss
- Labored breathing
- Poor capillary refill
- Poor posture
- Cachexia
- Altered mobility, gait
- Peripheral edema
- Cognitive impairment
- Chest pain

### Weight
- Take current weight and compare to pre – treatment or last recorded weight

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FATIGUE GRADING SCALE
Adapted NCI CTCAE (Version 4.03)

<table>
<thead>
<tr>
<th>Normal</th>
<th>GRADE 1 (Mild)</th>
<th>GRADE 2 (Moderate)</th>
<th>GRADE 3 (Severe)</th>
<th>GRADE 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td>Fatigue relieved by rest</td>
<td>Fatigue not relieved by rest, limiting instrumental ADL (e.g. preparing meals, shopping, managing money)</td>
<td>Fatigue not relieved by rest, limiting self care ADL (e.g. bathing, dressing, feeding self, using the toilet, taking medications)</td>
<td>—</td>
</tr>
</tbody>
</table>

*Step-Up Approach to Symptom Management:*
Interventions Should Be Based On Current Grade Level and Include Lower Level Grade Interventions As Appropriate

NORMAL– GRADE 1

NON – URGENT
Support, teaching, & follow-up as clinically indicated

**Patient Care and Assessment**
- Collaborate with physician to rule out other causes or concomitant causes of fatigue (e.g. Anemia) and to determine need for further investigation
  
  *Appendix A: Cancer and Treatment-related Anemia below*

**Patient Education**
- Reinforce that Cancer Related Fatigue is:
  - Normal, often treatable, and needs to be reported
  - Different than ‘normal’ fatigue and may not be relieved by rest
  - Not necessarily a sign of cancer progression or that treatment is not working

**Exercise**
- If recommending exercise, assess for facilitating/inhibiting factors, co-morbidities such as bone metastases, thrombocytopenia, anemia, fever, or active infection
- Set goals that are specific, achievable and realistic based on current health status
- Exercise during and after cancer treatment can result in more physical energy, improved appetite and increased ability to perform ADLs
- Start with light activity for short periods of time and encourage patient to gradually increase activity level to include 20 minutes (+) of endurance activities (e.g. walking, jogging, swimming) and muscle and bone strengthening activities 2x/week (e.g. light weights)

**Energy Conservation**
- Pacing
  - Balance activities with rest
  - Slow and steady pace uses less energy
- Planning
  - Organize your time, methods, and space
  - Encourage activities which are most enjoyed on days when feeling best
  - Develop a routine for rest and activity
- Priority setting
  - Eliminate unnecessary tasks, delegate responsibilities and ask for help
- Posture
  - Change positions frequently
  - Keep activities/work within easy range using correct body alignment
  - Avoid bending and lifting
- Proficiency
  - Use labour saving devices (e.g. elevator) to maximize efficiency and minimize workload
- Encourage self-monitoring of fatigue levels and patterns and times of peak energy

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### Sleep Hygiene
- **Encourage:**
  - Comfortable sleep surroundings
  - Soothing activities at bed time
  - Limiting naps to less than 1 hr
- **Avoid:**
  - Lying in bed at times other than sleep
  - Distracting noise (e.g. television, radio) during sleep
  - Caffeine and exercise near bedtime

### Dietary Management
- Encourage adequate hydration (e.g. 8 – 12 cups of fluid throughout the day). Caution in patients with co-morbidities that affect fluid balance (e.g. Congestive heart failure)
- Encourage adequate nutrition (e.g. high-protein diet)

### Pharmacological Management
- Avoid/discontinue any medications that may cause or exacerbate fatigue in collaboration with physician and pharmacist
- Medications may be prescribed to correct causative factors (e.g. iron supplement)

### Distraction and Relaxation
- Consider stress management, relaxation, distraction (e.g. music, games, reading, socializing)

### Follow-Up
- Re-assess at each visit and modify strategies as necessary
- Advise patient to contact healthcare providers if fatigue level increases or does not improve

### GRADE 2 – GRADE 3

#### URGENT:
Requires medical attention within 24 hours

### Patient Care and Assessment
- Collaborate with physician:
  - To rule out other causes or concomitant causes of fatigue
  - Need for further patient assessment at cancer centre or with GP
  - Special consideration for patients receiving Immunotherapy. Fatigue may not be a direct side effect of Immunotherapy, rather a product of immune mediated side effects. Refer to protocol specific algorithms for management.
- Monitor vital signs as clinically indicated
- Lab tests that may be ordered:
  - Complete blood count (CBC), electrolyte profile, transferrin, total iron-binding capacity, ferritin, iron levels, folic acid, B12 level, thyroid function tests,
  - AST / ALT, total bilirubin and evaluate endocrine function if patient on Immunotherapy

### Pharmacological Management
- Avoid/discontinue/reduce any medications that may cause or exacerbate fatigue in collaboration with physician and pharmacist
- Medications that may be prescribed:
  - Iron supplement
  - Psychostimulants (e.g. methylphenidate {Ritalin®} )
  - Sleep-enhancing medications (e.g. Benzodiazepines)
  - Blood transfusion or Erythropoiesis- Stimulating Agents (ESAs) such as Epoetin alfa or Darbepoetin alfa See Appendix A: Cancer and Treatment-related Anemia below
  - Corticosteroids (Refer to protocol specific algorithm if patient is on Immunotherapy)

### RESOURCES & REFERRALS

#### Referrals
- Patient Support Centre or Telephone Care Management
- Oncology Nutrition Services (Dietitian)
- Pain and Symptom Management/Palliative Care (PSMPC) - if multiple symptoms
- Physiotherapist
- Occupational therapy
- Patient and Family Counseling for stress management, relaxation, support groups
- Home Health Nursing

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## Immunotherapy
- **Immunotherapy Alert Card**
- Please refer to protocol specific algorithms to guide management of immune mediated side effects.

## Patient Education
- Patient Education Materials for Decreased Appetite: [http://www.bccancer.bc.ca/health-professionals/professional-resources/nutrition/nutrition-handouts](http://www.bccancer.bc.ca/health-professionals/professional-resources/nutrition/nutrition-handouts)
- Fatigue management video: Tired of Being Tired? [http://mediasite.phsa.ca/mediasite/Play/b5b255ef35384353811bdb150160a18a1d](http://mediasite.phsa.ca/mediasite/Play/b5b255ef35384353811bdb150160a18a1d)
- Cancer related fatigue patient education video [http://youtu.be/YTFPMYGe86s](http://youtu.be/YTFPMYGe86s) (open in chrome)

## Related Online Resources
- E.g. Fair Pharmacare; BC Palliative Benefits. Can be found in “Other Sources of Drug Funding Section” [http://www.bccancer.bc.ca/health-professionals/professional-resources/pharmacy/drug-funding](http://www.bccancer.bc.ca/health-professionals/professional-resources/pharmacy/drug-funding)

## Bibliography List
- [http://www.bccancer.bc.ca/health-professionals/professional-resources/nursing/symptom-management](http://www.bccancer.bc.ca/health-professionals/professional-resources/nursing/symptom-management)

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### Appendix A: Cancer and Treatment-Related Anemia

#### Definitions
- **Anemia:** Reduction in red blood cell mass, leading to a decrease in the hemoglobin concentration in the blood and reduced oxygen carrying capacity of the blood
- **Erythropoietin:** Hormone primarily made by the kidneys which stimulates the bone marrow to produce red blood cells
- **Epoetin alfa and Darbepoetin alfa:** Erythropoiesis-stimulating agents produced by recombinant DNA technology

#### Contributing Factors
- **Cancer – related:**
  - Highest for lung and ovarian cancer
  - Bone marrow infiltration
  - Hemolysis, blood loss associated with tumor
- **Cancer Treatment-related:**
  - Radiation therapy targeted at large areas of bone marrow
  - Myelosuppressive chemotherapy
  - Nephrotoxic effects of chemotherapy (e.g. platinum containing agents- Cisplatin)
  - Immunotherapy resulting in immune mediated hemolytic anemia
- **Other:**
  - Blood loss due to surgery, nutritional deficiencies, renal insufficiency, hypersplenism

#### Consequences
- Fatigue
- Impact on quality of life
- Impaired cognitive function
- May cause treatment delays and dose modifications
**ANEMIA GRADING SCALE (HgB levels in g/L)**
Adapted NCI CTCAE (Version 4.03)

<table>
<thead>
<tr>
<th>Normal Limits</th>
<th>GRADE 1 (Mild)</th>
<th>GRADE 2 (Moderate)</th>
<th>GRADE 3 (Severe)</th>
<th>GRADE 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women: 120-160g/L</td>
<td>100g/L-normal</td>
<td>80-100 g/L</td>
<td>&lt;80g/L Transfusion indicated</td>
<td>Life threatening consequences</td>
</tr>
<tr>
<td>Men: 140-180g/L</td>
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</tr>
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**ANEMIA ASSESSMENT AND MANAGEMENT**

**Patient Care and Assessment**
- Collaborate with physician to rule out other causes or concomitant causes of anemia (e.g. iron deficiency) and to determine need for further investigation
- Immunotherapy may result in hemolytic anemia via immune mediated side effects, collaborate with physician accordingly.
- Assess for:
  - Fatigue (focused assessment above)
  - Shortness of breath, dyspnea
  - Chest pain, rapid heart rate
  - Visible blood loss (e.g. urine, stool)
  - Previous blood transfusions. If so, note last date.
  - Headaches, dizziness, light headedness
  - Ankle swelling
  - Feeling cold, pale skin
  - Tinnitus
  - Activity level
- Monitor vital signs as clinically indicated
- Lab tests that may be ordered:
  - CBC, peripheral blood smear, vitamin B12 or folate levels, serum iron, transferrin and ferritin levels, reticulocyte count, erythropoietin level, direct and indirect Coombs test, and/or examination of a bone marrow aspirate and biopsy.

**Transfusion Therapy**
- Administer packed red blood cell transfusion as prescribed considering patient factors

**Radiation Therapy**
- May need urgent radiation if bleeding from a tumor

**Pharmacological Management**
- Medications may be prescribed to correct causative factors (e.g. iron supplement)

**Erythropoiesis stimulating agents (ESA)**
- Only recommended for anemic patients with cancer, who are receiving myelosuppressive chemotherapy and the intent of treatment is NOT curative
- Treatment should NOT be started until hemoglobin is LESS than 100 g/L
- The lowest dose needed to avoid RBC transfusions should be given
- ESAs should be discontinued at the end of chemotherapy treatment or if there is no response after 8 weeks of ESA therapy
- Iron supplementation may be considered to improve response to ESA therapy
- Risks of ESA include: increased mortality, tumor progression, thrombosis, cardiovascular events, hypertension, seizure and pure RBC aplasia
- Monitor iron levels before and during ESA treatment (majority of patients will eventually require supplemental iron therapy)
- Review with patient:
  - ESAs take at least 2 weeks to take effect
  - Ensure patient keeps appointment for blood work to monitor hemoglobin
  - Reinforce that BP needs to be measured and monitored
  - Importance of reporting symptoms (e.g. increased BP, headaches, confusion, seizures, weakness, edema, muscle aches, chest pain)

Protocol for the Use of ESAs:

**Follow up**
- Reassess symptoms and lab values at each visit
- Ask patient to contact healthcare providers if condition not improved or worsens and/or arrange a nurse-initiated telephone follow up

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