Fatigue: What It Is, What It Is Not, Why It Happens and What Can We Do about It?

Celebrating a Second Chance at Life
Survivorship Symposium

April 29 – May 5, 2023

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Memorial Sloan Kettering Cancer Center
Learning Objectives

• What causes/contributes to fatigue in the short- and long-term after stem cell transplant
• The difference between normal fatigue and fatigue experienced by stem cell transplant recipients
• Strategies to conserve energy and plan a day to minimize the impact of fatigue on daily life
• Role of exercise, sleep and nutrition in managing fatigue
• Pharmacological and non-pharmacological options for managing fatigue
Cancer-Related Fatigue (CRF)

- Patient perspective:
  - “Rest does not make it go away, and just a little activity can be exhausting”
- Physician Perspective
  - Etiology “remains to be fully elucidated”
- Bottom line
  - Patients have trouble making things happen
Making Things Happen: the Bird's-Eye View

Problems can happen

- Exercise
- Running
- Planning
- Cooking
- Sleeping
- Eating
- Drinking
Making Things Happen: The Energy Coin

- Mental Effort
- Power Burst
- Sustained Effort

ATP = Adenosine Triphosphate
Minting the Energy Coins
### What is the Cost of Daily Functions?

<table>
<thead>
<tr>
<th>Activity</th>
<th>Energy Cost (METS)</th>
<th>Oxygen use VO₂ (ml/kg/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doing nothing</td>
<td>0.7-1</td>
<td>3.5</td>
</tr>
<tr>
<td>Standing still</td>
<td>1.6</td>
<td>5.6</td>
</tr>
<tr>
<td>Making a bed</td>
<td>3</td>
<td>10.5</td>
</tr>
<tr>
<td>Walking ~ ½ normal speed</td>
<td>3.2</td>
<td>11.2</td>
</tr>
<tr>
<td>Walking briskly</td>
<td>4.28</td>
<td>15.0</td>
</tr>
<tr>
<td>Ascending stairs</td>
<td>4.77</td>
<td>16.7</td>
</tr>
</tbody>
</table>

Knaggs, 2011; Mansoubi 2015

15.4 ml/kg/min
Warburg Effect: Messing Up the Energy Coin Mint

- Cancer cells prefer a very inefficient way of making ATP, using a lot of glucose
- Reason why PET scans work
- Cancer may shift the rest of the body into a less efficient mode
  - 2 ATP's from 1 glucose, instead of 36
Where The Coins Are Used: Muscle Fibers

Type I “Keep Going” Fibers

Type IIa “Keep Going Strong” Fibers

Type IIb “Do It Once” Fibers
Chemotherapy Effects on Muscle

Direct Damage
Loss of "Power" Fibers
Secondary muscle loss due to neuropathy

Damage lasts longer when muscle is already injured

Muscle Weakness Fatigue
↓ Muscle Fiber Strength
↓ Muscle Fiber Endurance

↑ Inefficient work
↑ Muscle cell death
Mitochondrial damage (↓ ATP/Energy Coins)

ATP = Adenosine Triphosphate
Bed = Bad (Even for Healthy Folks in Space Program)

~5% loss of muscle strength per week
~3% loss of muscle size per week

More prone to dizziness after as little as 24 hours
Large leg muscles go first

Body at rest remains at rest

Brown, 2009; Hortobágyi, 2000; Berg, 1985
What Cancer-Related Fatigue IS NOT

- Cancer-Related Fatigue IS NOT
  - Character flaw or personal weakness
  - Stimulant medications have a very small effect (<10%)
  - “Primary interventions should be exercise, psychological, or exercise plus psychological”

“‘I’m just lazy’
‘I’m just not working hard enough’”

Mustian, 2017
Mindset

• Don't dwell on what you can't or didn't do
• Start low, go slow, try to stay consistent
• No task accomplished is too small to recognize, especially early in the journey
• Set sights on the future
• Track your progress

Amonoo, 2021
Mindfulness (Conscious Breathing)

• 10 minute preparation
  • Concentrate on lower abdomen 3 min
  • Place left ankle over right knee 2 min
  • Place right ankle over left knee 2 min
  • Bend both knees 2 min
  • Relaxation breathing 10 minutes

• 10 minute finish exercises
  • Relax body and mind
  • Stroke face and hair
  • Rotate ankles
  • Stretch arm and legs
  • Stretch out on the bed

Kim, 2006
Mindfulness (Conscious Breathing)

White Cell Count after 6 weeks

- Exercise (1000*Cells/ml)
- Control (1000*Cells/ml)

Before
35 donor cell transplant recipients, ~ 33 yo,
South Korea

After

Kim, 2006
Exercise: Why Spend More Coins If You Already Feel Short?

Effects of 6-Week Treadmill Walking

- Training Speed (mph)
- Max Distance (mi)
- Max Speed (mph)

20 Transplant Patients (17 donor, 3 own)
36 yo, 18-42 days after transplant

Dimeo, 1996
Can Exercises Be Harmful During Treatment?

• No side effects from exercise participation
• Increased physical function score
• Increased endurance
• Decreased fatigue scores
• Fewer days with nausea

• 10-20 cycling
• 20 minutes resistance OR
• 20 minutes activities of living

Dimeo, 1999; Baumann, 2011; Oechsle 2014;
Can Unsupervised Exercise be Effective?

- 17 Floridians, ~ 49 yo
- ~16 months after transplant
- 13 own cells, 4 donor cells
- At least 3 times/week
- At least 20 minutes moderate intensity per heart rate monitor

Wilson, 2005

~ 15% gain = became 15 years younger
Can Exercise Be Helpful if You're REALLY tired?

- 12 Canadian patients, ~49 yo
- ~ 39 months after donor cell transplant

- 20 minutes 2/10 effort
- 15 minutes 6/10 effort
- 20 minutes 4/10 effort  X 12 weeks

**Bonus:** Aerobic fitness improved 17%
(folks got ~ 17 years younger)

Carlson, 2006
What About Both Physical Exercise and Mindfulness?

- 21 Australians, ~ 56 yo
- ~37 months after donor transplant
- 6 weeks of virtual coaching
  - 60 min physical
  - 60 min mindfulness
- 20-30 min aerobic exercise
- Resistance bands workout
- 3-5 times per week

~ 27% gain = became 27 years younger

Aerobic fitness

Ma, 2022
Fueling Up

• Mouth can be sore
• Taste can be altered
• Nausea happens almost universally
• Food intolerances may develop
• Stomach and intestines can be affected by graft-versus-host disease (GI GvHD)

• Acupressure for nausea can be helpful
Resting Up

- Biggest Problem: transplant admission
- Donor cell transplant recipients tend to fare worse
- ~1/3 of all remain affected

Sleep is a Habit that needs good maintenance

Prevalence of Insomnia in Transplant Recipients

- Germany
- Turkey

Rischer, 2009; Yavulal, 2022; Cancer.org
Our Approach: CHEAP-O Exercises Only (Sit-To-Stands for All)

- **Cost nothing**
- **Have meaning**
- **Easy and safe**
- **Adaptable**
- **Portable**
- **Outcome-friendly**

**Predicts**
- Mortality
- Older men,
- Lung disease

**Correlates**
- With walk test
- Head and Neck cancer

**Improves**
- With training
- Prostate Ca

**Correlates**
- With CRF
- Breast Ca

**Correlates**
- With QoL Step Test
- HSCT

**Chair Rise Test**
(Sit-To-Stand)

De Buyser, 2013; Puhan, 2013; Eden, 2018; Gaskin 2016; Cuesta-Vargas, 2019; De Almeida 2019; Azzi 2021
**High-Intensity Interval Training (HIIT)**

**Tabata Protocol**
- Go at 90% capacity
- Work 20-30 sec, rest 10 sec
- Repeat 16-12 times

**Meyer Protocol**
- Go at 85% capacity
- Work 30 sec, rest 60 sec

Safe and Effective after heart surgery and in heart failure

Can Interval Training be safely applied to cancer patients? **YES!**


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**Scientific 7 Minute Workout**
Non-negotiable Exercise Rules

1. If it hurts when you do it, don’t do it (but mild discomfort is OK sometimes).
2. Don’t work too hard – your effort or exertion level should almost never come up higher than 6 on a 0-10 scale (0 – no effort, 10 – absolute hardest, all-out effort). Exercise should not make it impossible to do other things later in the day.
3. Don’t do things you regret. For example, if you’ve done something that leaves you sore or overly tired the next day, don’t repeat it.
How To Get Started With Sit-To-Stand Training

1. Find a **comfortable seat height**: safely get up and sit down without arm help
2. Count how many times you can get up and sit down in 30 seconds, effort less than 6 out of 10 (0 – no effort, 10 – all-out effort).

**Results:**
- 5 repetitions or less
- **OR**
- The seat height is much greater than a normal chair

**Sunrise-Sunset**

**Results:** 6-10 repetitions

**Breakfast-Lunch-Dinner**

**Results:** 10 or more repetitions

**Interval Training**
- Every Minute
- On the Minute (EMOM)

2023 SURVIVORSHIP SYMPOSIUM
Sunrise-Sunset Sit-To-Stand Training

- You are in the Sunrise-Sunset group if you need a seat much higher than a regular chair (similar in height to your bed) or did 5 or fewer repetitions during the test.
- You can practice sit-to-stands in the morning and at night, when you are next to the bed.
- For example, a person who did 3 sit-to-stands will start with just 1 repetition per workout and advance as per table to the right.
- Goal: 15 reps per set

<table>
<thead>
<tr>
<th>Day</th>
<th>Sunrise</th>
<th>Sunset</th>
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</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>1</td>
<td>1</td>
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<td>Day 2</td>
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<td>Day 8</td>
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<td>Day 9</td>
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<tr>
<td>Day 10</td>
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<td>6</td>
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</tbody>
</table>
Breakfast-Lunch-Dinner (BLD) Sit-To-Stand Training

- You are in the BLD group if you did between 6 and 10 repetitions during the test.
- You can practice sit-to-stands 3 times per day: breakfast, lunch, and dinner.
- Take half of the test result and round it down. For example, a person who did 9 sit-to-stands will start with 4 repetitions per workout and advance as per table to the right.
- Goal: 15 reps per set

<table>
<thead>
<tr>
<th>Day</th>
<th>Breakfast</th>
<th>Lunch</th>
<th>Dinner</th>
</tr>
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<tbody>
<tr>
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<td>Day 10</td>
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</table>
Every Minute on the Minute (EMOM) Sit-To-Stand Training

- You are in the EMOM group if you did more than 10 repetitions during the test.
- Take half of the test result and round it down. For example, a person who did 11 sit-to-stands during the test will start with 5 repetitions per set and advance as per table to the right.
- Warm-up then set a timer for 5 1-minute sets and do the prescribed number of sit-to-stands at the beginning of every minute.
- Goal: 15 reps per set

<table>
<thead>
<tr>
<th></th>
<th>Set 1</th>
<th>Set 2</th>
<th>Set 3</th>
<th>Set 4</th>
<th>Set 5</th>
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</tbody>
</table>
Case Study: Setting Goals and Keeping Track

• 61 yo readmitted with severe GI GvHD 1 month after donor cell transplant.

• 7 month stay, multiple infections, loses A LOT of muscle, suffers recurrent back pain.

• **Goal:** dance at a wedding in 3 months
### Staying Accountable – "Not For Everybody"

#### THERE'S NO SUCH THING AS A BAD DAY!

<table>
<thead>
<tr>
<th>Day</th>
<th>Time</th>
<th>Activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>D</td>
<td>7:00</td>
<td>Wedding Dance A</td>
</tr>
<tr>
<td></td>
<td>8:00</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>9:00</td>
<td>#</td>
</tr>
<tr>
<td>S</td>
<td>6:30</td>
<td>BackPain #6</td>
</tr>
<tr>
<td></td>
<td>7:00</td>
<td>BackPain #6</td>
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<td></td>
<td>8:00</td>
<td>BackPain #6</td>
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<td>9:00</td>
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<td>10:00</td>
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<td>BackPain #7</td>
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<td>6:30</td>
<td>BackPain #8</td>
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<td>F</td>
<td>6:30</td>
<td>BackPain #8</td>
</tr>
</tbody>
</table>

#### 2023 SURVIVORSHIP SYMPOSIUM
### Sloan BLD Circuit Sit-To-Stand Rules:
1. Nothing should hurt in the process. Up and down movement is smooth - no bouncing or lurching.
2. Seat has to be high enough to perform sit-to-stand comfortably with as little assistance as possible.
3. Keep the seat at the same height until you can do 3 sets of 30 reps with effort < 5.
4. At the end of each set, should not feel more than “pleasantly tired.”
5. Don’t advance until the last set feels no harder than the first set and effort is less than 5/11.
6. Start writing down heart rate once you feel that it goes up after a set.

<table>
<thead>
<tr>
<th>Date</th>
<th>Seat Height, In or Cm</th>
<th>Start Heart Rate</th>
<th>B'Fast</th>
<th>Lunch</th>
<th>Dinner</th>
<th>End Heart Rate</th>
<th>Effort (0/easy - 10/very difficult to pass out)</th>
</tr>
</thead>
<tbody>
<tr>
<td>11-12-22</td>
<td>23.7</td>
<td>119/71</td>
<td>6/2</td>
<td>127/60</td>
<td>117/75</td>
<td>122/72</td>
<td>2-1</td>
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<td>11-12-22</td>
<td>24.7</td>
<td>119/71</td>
<td>6/2</td>
<td>127/60</td>
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<td>122/72</td>
<td>2-1</td>
</tr>
</tbody>
</table>

60 days training: sit-to-stands improved.
28” seat became 22” seat.
3 repetitions improved to 14.
Take Home Points

• Difficulty getting things done after a stem cell transplant comes from the effects of disease and treatment

• Difficulty getting things done after a stem cell transplant is not a character flaw or a personal weakness

• Start low, go slow, stay consistent, track your progress and recognize your accomplishments

• Don't work too hard (keep effort less than 6 on a 0-10 scale) and don't work through pain (though minor discomfort is OK)

• Make your bed, brush your teeth, stay hydrated and talk to your team

• Sleep is a habit that may take time to build
MSKCC Exercise Videos

Breathing Video:

• https://www.mskcc.org/cancer-care/patient-education/breathing-exercises-01

Chair and bed exercise videos:


• https://www.mskcc.org/cancer-care/patient-education/beginner-bed-exercises-01

• https://www.mskcc.org/cancer-care/patient-education/intermediate-bed-exercises-01

• https://www.mskcc.org/cancer-care/patient-education/advanced-bed-exercises-01
Thank you!

• Questions?
• Comments?
• Jokes?
• Tweet @RehabGrisha @CancerRehabDocs
• Visit: https://health.gov/our-work/nutrition-physical-activity/move-your-way-community-resources
QUESTIONS?

Grigory (Grisha) Syrkin MD
Memorial Sloan Kettering Cancer Center
LET US KNOW HOW WE CAN HELP YOU

Visit our website:  bmtinfonet.org

Email us: help@bmtinfonet.org

Phone: 888-597-7674 or 847-433-3313

Find us on:

Facebook, facebook.com/bmtinfonet

Twitter, twitter.com/BMTInfoNet
References


References


References


References


References


• Reynolds G. The Scientific 7-Minute Workout. https://well.blogs.nytimes.com/2013/05/09/the-scientific-7-minute-workout/ (Last Accessed: 03/22/2023)
