CANCER SURVIVORSHIP AND WOMEN’S HEALTH: WHAT ARE THE CHALLENGES?

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Number of Cancer Survivors

There were estimated to be 13.7 Million Cancer Survivors in the United States as of January 1, 2012. This represents approximately 4% of the U.S. population.

NCI/Office of Cancer Survivorship
http://dccps.cancer.gov/ocs/

Cancer Survivor Facts

- 60% of survivors are currently over the age 65 years.
- Breast, Prostate, and Colorectal, are the 3 most prevalent cancer sites.
- Approximately 14% of the 13.7 million estimated cancer survivors were diagnosed over 20 years ago.
- The current average age of male and female cancer survivors is 69 and 64 respectively.

American Cancer Society
Public Service Advertisement
ca. 1988

More people have survived cancer than now live in the City of Los Angeles.
Estimated number of cancer survivors in the United States as of January 1, 2012 by cancer site.


Estimated number of cancer survivors in the United States as of January 1, 2012 by time since diagnosis and sex.


How did we make such incredible strides?

- Earlier detection
- New drugs and other treatments
- Combined modality therapy
- Prolonged adjuvant and/or maintenance therapies
- Prevention of second malignancies

But there is a cost...

- Time
- Money
- Human
- Interpersonal
- Existential

Breast cancer as a model for study of late effects...

- Most common cancer in women
- Occurs across the lifespan
- Complex treatments, with high rate of cure
- Treatment affects menopausal status and endocrine milieu of the woman
- Potential for substantial impact on physical and emotional health
### 2000 NIH Consensus Conference

- Adjuvant chemotherapy recommended for all women with tumors > 1 cm
- Adjuvant endocrine therapy advised for all women with tumors that contain hormone receptors
- Although patients with tumors < 1 cm will benefit from treatment, the toxicity may outweigh the absolute benefit
- Today, this is modified by examination of tumor gene expression profiles, so we avoid chemotherapy in many patients

### Concerns voiced by women at the end of treatment....

- How will I know if my treatments worked?
- When will I get my energy back?
- What is the follow-up plan now that my treatments are over?
- Does this new ache mean that the cancer is coming back?
- Why does my family think that everything is okay now when I know it isn’t?

### Changes in Physical Functioning

- Cardiorespiratory symptoms – CHF
- Fatigue – multi-factorial
- Cognitive dysfunction - late effect of cancer treatment
- Sexual and urinary problems – secondary to chemotherapy or hormonal changes

### Other Medical Late Effects

- Lymphedema – critical need for prevention and intervention strategies
- Premature menopause
- Infertility
- Osteoporosis/fractures – need for preventive strategies
- Chronic pain; scars; body changes

### Psychological Late Effects

- Depression, sadness
- Inability to make plans
- Concerns about the future or death
- Health worries
- Sense of self-esteem and mastery
- Uncertainty and vulnerability
- Feelings of gratitude and good fortune

### Intersection of Menopause & Breast Cancer Treatments

- Healthy women have age-related changes in symptoms and QOL
- Breast cancer treatments exacerbate common symptoms of menopause and aging
- Infertility and/or transient amenorrhea
- Premature menopause
- Menopause related syndromes: vasomotor symptoms, vaginal dryness and urinary symptoms, bone loss and fractures
Menopausal Symptoms & Age in Healthy Women Entering BCPT (P-1)

HOT FLASHES BY AGE GROUP

VAGINAL DRYNESS BY AGE GROUP

PAIN WITH INTERCOURSE BY AGE GROUP

JOINT PAINS BY AGE GROUP

Treatment related long-term effects

- Symptoms that start while on treatment and persist beyond the end of treatment, e.g., fatigue or cognitive complaints
- Treatment intensity, not related to a specific drug
- Unique to a specific drug, e.g., taxane neuropathy
- Premature menopause is a major burden for younger women receiving chemotherapy
- Ongoing endocrine therapy related problems, e.g., AI associated vaginal dryness and musculoskeletal complaints
Cancer-related Fatigue

- Fatigue is the most common side effect of cancer and its treatment
  - Occurs in 60 – 96% of patients during treatment (Wagner & Cella, 2004)
  - Fatigue may persist for months or years after successful treatment completion
  - 30% of breast cancer survivors report fatigue 1-5 years post-diagnosis (Bower et al., 2000)
  - 63% of fatigued survivors continue to report fatigue 5-10 years post-diagnosis (Bower et al., 2006)

Description of Cancer-related Fatigue

- Different than “normal” fatigue due to lack of sleep or over-exertion
- More pervasive, debilitating, longer-lasting
- Involves physical, mental, emotional components
- Not relieved by adequate sleep or rest

Etiology of Cancer-related Fatigue

- Fatigue occurs across different types of cancer and different types of cancer treatment
- Mechanisms underlying cancer-related fatigue have not been determined

What causes fatigue?

- Demographic factors
  - Age
  - Income
  - Marital status
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Demographic factors
- Age
- Income
- Marital status

Psychosocial factors
- Depression
- Catastrophizing coping style

Health behaviors
- Physical activity

Comorbid medical conditions
- Cardiovascular disease
- BMI

Biological factors
- Anemia
- Inflammation

Comorbid symptoms
- Pain
- Menopausal sx
- Sleep disturbance

Health behaviors
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**Inflammation**

- Body's response to infection or injury
- Mediated by proinflammatory cytokines
  - IL-1β, IL-6, TNF-α
- Local and systemic effects, including effects on CNS

**Design of the UCLA Mind Body Study**

**Longitudinal Cohort Study**

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<th>Blood collection</th>
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<td>0 months</td>
<td>6 months</td>
<td>12 months</td>
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<td>MP testing &amp; Self-report (PET scan, subtraction)</td>
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**sTNF-RII Change over 1 year by Chemo Status (n=93)**

- **Chemotherapy**: p<0.01
- **No Chemotherapy**: p=0.29

**As TNF declines, there is improved prefrontal activity**

**Associations between three individual SNPs in the promoter regions of these cytokine genes and severity of fatigue and cognitive complaints at baseline (n=171)**
Additive Genetic Risk Score for These SNPs

- Patients with more high expression alleles have more severe fatigue and cognitive complaints
- Genetic risk index is significantly associated with greater fatigue and cognitive changes

Bower et al., JCO, 2013

Vulnerability factors:

- Depression
- HPA axis dysregulation
- Cytokine gene polymorphisms

Cancer and cancer treatment

Inflammation

FATIGUE

Immune and neuroendocrine changes:

- Alterations in cellular immune system
- Alterations in HPA axis function

Bower Model—Brain, Behavior and Immunity, 2007

Late Effects of Systemic Therapy

- Interaction with co-morbid conditions
- Interaction with other treatments, e.g., radiation and cardiac effects
- Second malignancies, e.g., leukemia
- Menopause-related, e.g., bone health
- Accelerated aging, e.g., cognitive decline, congestive heart failure

Subpopulations of Breast Cancer Survivors

Time to Remove the Subspecialty Blinders: Breast Cancer Does Not Exist in Isolation

Most women with breast cancer will die from comorbid conditions.....

Competing Causes of Death From a Randomized Trial of Extended Adjunctive Endocrine Therapy for Breast Cancer

Menopause-related, e.g. bone health

Accelerated aging, e.g. cognitive decline, congestive heart failure

Most women with breast cancer will die from comorbid conditions.....