Long-term effects of chronic GVHD in adults

Bipin Savani
Transplant Activity in the U.S.
Transplant Activity in the Europe

EBMT data. BMT Long Term Management: Prevention and Complications 2013
Improving transplant outcome

One-Year Survival, percent

- HLA-matched sibling
- URD

Better supportive care
Gentler conditioning
Improved mgmt of GVHD

Pasquini MC, Wang Z. CIBMTR
Long-term Follow Up after SCT

- First successful transplants – late 1960’s and early 1970’s
- Improvements in SCT outcomes resulted in a larger number of cure patients
  - >30,000 Patients >5 years from SCT
  - Increasing annually
- As they age, more attention must be paid to long-term complications
Long term stem cell allotransplant survivors are a growing population

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approximate number of allotransplants in the last 30 years</td>
<td>450,000</td>
</tr>
<tr>
<td>50% Average survivorship per annum</td>
<td>225,000</td>
</tr>
<tr>
<td>Projected number of new long term survivors generated 2020 (conservative)</td>
<td></td>
</tr>
<tr>
<td>Assume 5% increase / annum 10 years</td>
<td>320,000</td>
</tr>
<tr>
<td>Assume average survival over the decade</td>
<td>255,000</td>
</tr>
<tr>
<td>Estimated worldwide allogeneic transplant survivors by 2020</td>
<td>~ 500,000</td>
</tr>
<tr>
<td>Estimated US population of allogeneic transplant survivors by 2020</td>
<td>~140,000</td>
</tr>
</tbody>
</table>

How I treat late effects in adults after allogeneic stem cell transplantation. Blood 2011
Semin Hematol 2012
Long-term Survival after HCT

- CIBMTR study of 10,632 allogeneic HCT recipients surviving ≥ 2 years in remission (median follow-up 9 years)

Overall survival vs. Non-relapse mortality

J Wingard et al, JCO 2011; 29: 2230
Long term transplant clinic - checklist

**DISEASE** - restaging, TKIs/ hypomethylating agents, etc

**cGVHD** - activity versus sequelae

**IMMUNE RECONSTITUTION** - reimmunization status, infection risks

**SEQUELAE** - pulmonary & metabolic (CV), endocrine, ophthalmic, fertility

, iron, bone health, cognition & mental health, renal, sexual dysfunction

**GENERAL HEALTH** - Secondary cancers

*Common and serious; *Uncommon but life threatening; *Common but not life threatening
Timelines for post SCT complications

- A-GVHD
- C-GVHD
- Viral reactivation
- Relapse
- Early TRM

Years:
- 1
- 3
- 5
- 10
- 15
- 20

Complications:
- Thyroid failure
- Male fertility
- Cataract surgery
- Bone loss / premature ageing
  - Cardiovascular
  - Pulmonary
- Second cancers

QOL & ??
What goes wrong: the next 3 years

- Graft Failure
- Relapse
- Transplant-related complications- cGVHD
  - Hepatic, skin, musculoskeletal, BOOP
  - Limited lifestyle
- Immunodeficiency
  - VZV, Pneumococcus/ hemophilus etc

- Conditioning regimen-related problems
What goes wrong: the next 30+ years

- Late effects
  - Metabolic complications
  - Pulmonary complications
  - Bone loss/ AVN
  - Delayed immune reconstitutions
  - Renal complications
  - IQ, cognitive problems
  - Second malignancies
  - Lifestyle
  - Lifespan
  - Premature aging?
Immune dysfunction underpins many late effect complications

- Conditioning regimen
- Pre-transplant/genetic predisposition
- Iron Overload

- Thyroid failure
- Endocrine failure
- Cataracts

- Infection

Chronic GVHD
cGVHD $\iff$ Immune dysfunctions and Infections
Delayed immune recovery

- B cells and immunoglobulins
- Platelets
- Neutrophils
- Thymic derived lymphocytes
- CD4
- CD8
- Clonal expansions
- Normal immunoglobulin levels
- NK
- 20,000/cu mm
- 500/cu mm

3 weeks
3 months
3 years

3 weeks
3 months
3 years

Delayed immune recovery
Defects in humoral immunity

- Hypogammaglobulinemia is common
  - Normal or near normal values do not necessarily mean protective level of IgG
- Apparently normal IgG levels may obscure low IgG2 and IgG4 needed to clear encapsulated organisms
- Low secretary IgA
  - Increase susceptibility to conjunctivitis, sinusitis, bronchitis, etc.
- Loss of splenic function
- May require long-term prophylaxis with antibiotics designed to prevent pneumococcal disease
  - Increasingly problematic as the bacteria develop antimicrobial resistance
Defects in cellular immunity

- Varicella-zoster reactivation is 20-50%  
  - ~10% of cases → pain without rash

- Cytomegalovirus  
  - First 3-4 months after SCT  
  - Late infections may be increasing with pre-emptive therapy

- PCP  
  - >1 year after SCT  
  - Continued immunosuppression requires sustained prophylaxis  
  - Daily bactrim prevent PCP and reduce the risk of pneumococcal sepsis and toxoplasmosis
Infection- pneumococcal sepsis after SCT

higher probability of pneumococcal infection among allograft recipients

- No pneumococcal vaccine
- PCN or Ery (compliance not monitored)
  - Pneumonia 16
  - Bacteremia alone 19
  - With meningitis 3
  - With pneumonia 3
- 23% mortality

Significantly higher risk for pneumococcal sepsis among allograft recipients with chronic graft versus host disease

Anti-infective prophylaxis

- Antifungal- if on systemic IST, particularly steroids, iron overload

- ACV- for VZV at least 1 year post cessation of IST. Varicella-zoster reactivation is 20-50%. ~ 10% of cases → pain without rash

- PCN- vs. encapsulated (while on IST)

- PCP prophy- At least 6 months post cessation of IST
# Vaccination schedule

## Table II. Immunizations Post Allogeneic Transplant

<table>
<thead>
<tr>
<th>Type</th>
<th>3-6 Mo</th>
<th>12th Mo</th>
<th>14 – 18 Mo</th>
<th>24 Mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza Virus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lifelong, seasonal, starting before HSCT and resuming after 6 months</td>
<td></td>
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</tr>
<tr>
<td>Pneumococcal 13-valent conjugate (0.5 mL, IM)</td>
<td>X</td>
<td>X</td>
<td>X (18 mo)</td>
<td></td>
</tr>
<tr>
<td>Pneumococcal 23-valent Vaccine (0.5 mL IM)</td>
<td></td>
<td></td>
<td></td>
<td>Xg</td>
</tr>
<tr>
<td>DTaP a (0.5 mL IM)</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Hib b conjugate (0.5 mL IM)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>IPV c (0.5 mL SQ or IM)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Hepatitis A (1 mL IM in adults or 0.5 mL IM in children up to 18)</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis B (1 mL IM)</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Meningococcal d (0.5 mL SQ)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMR e (0.5 mL SQ)</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>VZV f (0.5 mL SQ)</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

CDC/ASBMT guidelines 2012. NIH BMT CONSORTIUM 2013
Updated vaccination recommendations

**ACIP recommendations for pneumococcal vaccines (June 2012)**
- Fifty percent of invasive pneumococcal disease cases were caused by serotypes contained in PCV13 (Prevnar); an additional 21% were caused by serotypes only contained in PPSV23 (Pneumovax) (CDC, unpublished data, 2011).

- New vaccination guidelines recommend three doses of Prevnar followed by one dose of Pneumovax in allogeneic transplant recipients.

CDC 2012
Cardiovascular complications

**Events:** CAD, CVA >> PAD

**Magnitude:** CVD is 3-fold higher than sibling controls

**Risk factors:** dyslipidemia-driven

**Etiology:** XRT, steroids, endocrinopathy

**Management:** address modifiable factors (lipids, DM, HTN, smoking)

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Rovo A, Tichelli A. BMT Long Term Management: Prevention and Complications 2013
Rovo et al. Semin Hematol 2012
Dyslipidemia after allo-HCT. Blood 2010
Cardiovascular complications

Primary disease

Comorbidity

familial risk factors

Pre-HSCT exposure:
- radiation
- Comorbidity

HSCT

Conditioning
GVHD

De novo CV risk factors

Clinical event

Cardiovascular disease

Vascular endothelial lesions

Enhancement of atherosclerosis

Premature atherosclerotic process

Rovo A, Tichelli A. BMT Long Term Management: Prevention and Complications  2013
• Dyslipidemia in 44% and 52% at 5 and 10 years post-SCT.

• 23% of 5-year survivors met the ATPIII threshold for dyslipidemia treatment.

• Increased prevalence of hypertension (p<0.001), diabetes (p=0.018) and BMI (p=0.044) compared to baseline.

• The Framingham general CV risk score (FGCRS) in males at 5 years post-SCT projected a doubling (10.4% vs. 5.4%) in the 10-year risk of cardiovascular events.

• Elevated CVRF stabilized between 5 and 10 years post-SCT but.

Dyslipidemia after allo-HCT. Blood 2010
Pulmonary complications

Cumulative pulmonary injury 30-60%
Impact of cGVHD on the time to PFT decline

Biol Blood Marrow Transplant. 12:1261-9; 2006
Bronchiolitis Obliterans Syndrome

- **Facts**
  - Insidious, 2-5 years.
  - ~15% of cGVHD.
  - High morbidity and mortality
  - In lung transplantation, affects 50%.
  - Small airway narrowing \(\rightarrow\) 45% of terminal bronchioles lost before

- **Diagnostic criteria:**
  - Decreased FEV1 <75%, AND FEV1/FVC ratio of <0.7 on PFT
  - RV >120% OR air trapping on computed tomography or lung biopsy
  - Absence of acute respiratory infection AND
  - cGVHD in an additional organ system if no histologic evidence of BOS can be demonstrated
Prevention & Therapeutic Strategies

- Aggressive GVH prophylaxis (ATG) in patients with pre-transplant abnormal PF- goal to prevent cGVHD (BMT 2013 in press).
- Inhaled steroids
- Azithromycin
- FAM (fluticasone/azithro/monteleukast)
- Investigational therapy- inhaled cyclosporine
- Lung transplantation

Biol Blood Marrow Transplant. 2012;18:1479-87
Bone health - Avascular necrosis

- Incidence 4-19%
- Hips > knees, ankles or shoulder
- Sometimes infected. Often excruciating.
- Median at 2 years
- IST use, mainly steroids (ALL, female)
- MRI – most sensitive + extent of involvement
- Mx: Conservative
  - Reduce wt bearing
  - Surgical
    - core decompression ->
    - joint replacement
- No role for statins or bisphosphonates!
Definitions: Osteopenia (T-score between -1.5 and -2.5) and osteoporosis (<-2.5 or fragility frx)

Features: Bone loss occurs in 50-60%
- ~ 20% develop osteoporosis
- Children >> adults (but no fractures)
- Trabecular bone (hip & spine) are more susceptible.
- Commonest fracture site is femoral neck.
- Extremely rapid in the first 4 months (~7-10 years of normal aging)

Risk factors: Steroids, hypogonadism, Vit D (diet, renal), RANK-L, inactivity

Screening: DEXAs, Vitamin D levels

Management: Calcium (1,200 mg daily)/ vitamin D (1,000 IU/d), exercise, bisphosphonates (individualize- risk of osteonecrosis, drug holiday reqd after 3-5 yrs), HRT for all females at risk, role of androgens is unknown. Denosumbab is untested.
Bone Loss and cGVHD

![Graph showing bone density over age and months post-transplantation]

- Normal score
- Osteopenia
- Osteoporosis

Graph A: T Score vs. Age (years)
- Male (gray)
- Female (red)

Graph B: T Score vs. Months post-transplantation
- On IST (red)
- no cGVHD (gray)
- History of cGVHD (diamonds)
DM: risk is 3x that of sibling controls
- cGVHD, TBI, steroids. HbA1c is unreliable. Oral hypoglycemics often CI

Male hypogonadism:
- Testosterone producing Leydig cells less damaged than sperm producing Sertoli.
- Recovery of spermatogenesis in 50-90% of non-TBI and ~ 25% of TBI survivors.
- Supplement testosterone very selectively - low morning total testosterone level AND reduced libido/bone mass. Monitor LFTs, PSA and HCT

Thyroid:
- ~ 30% of pediatric patients followed long term – TBI & cGVHD.
- TSH elevations are initially subclinical. Rx- lifelong supplementation.
- Thyroid adenomas and carcinomas may occur at higher rates than expected (XRT)

Adrenal Insuff:
- Overt or ACTH challenge. High prevalence (19 of 20 in one series). QOD steroids.

Pituitary:
- Growth failure, central hypogonadism or hypothyroidism.
- TBI, young age at BMT
- 40/141 children failed to achieve normal adult height.
- Growth charts
Thyroid functions in long term survivors

Age and overt hypothyroidism

Prolonged IST and hypothyroidism

Graph A:
- Proportions of patients (%)
- Time to hypothyroidism (months)
- Oldest quartiles (26.5±10.2%) (median age 47, range 44-66)
- First 3 quartiles (7.4±3.5) (median age 32, range 6-43)
- p=0.026

Graph B:
- Proportions of patients (%)
- Time to hypothyroidism (months)
- (11/14 patients on prolonged IST)
- p<0.0001
- Not on prolonged IST (30.3±5.9%)
Estimates of CKD in HCT survivors vary from 13% to 66% for adults and 62% in children.

Often delayed up to 10 years post transplant.

CKD defined as a sustained elevation of serum creatinine (GFR < 60 mL/min/1.73 m2) for 3 months or longer

Mx: HTN, Renal fxn, exclude obstructive uropathies, renal biopsies for etiology.
Ophthalmic complications

- #1 cGVHD
- #2 Cataracts
- Others: xerophthalmia w/o cGVH, corneal ulcers, glaucoma, CMV retinitis, fungal endophthalmitis, donor allergy.
- The cumulative incidence of major ocular complications - 13%
- cGVHD
  - Lacrimal, conjunctival, lids, cornea.
  - Sicca
  - Rx: Artificial tears → topical CSA/steroids → plugs → punctal cautery → autologous serum
- Premature Cataracts
  - 23% in pediatrics
  - Steroids and TBI (lens shielding)
  - Rx: aggressive management of dry eyes
Female long term survivors

- cGVHD- vulvar and vaginal
  - 25-50%. Underreported
  - Vulvar starts in 1\textsuperscript{st} year but vaginal
  - may present several years later
  - Severest form- hematocolpos
  - Regular mandatory GYN screening reduces surgery
  - Rx: Topical IST, estrogens, dilators

- HRT and contraception
- HPV-related cervical dysplasia
- Infertility
- Sexual health
- Hypogonadism

BMT Long Term Management: Prevention and Complications 2013
Shanis et al. Semin Hematol 2012
Iron Overload

- 30-60%, easy to overlook. Sole pathologic finding in one third of liver biopsies.
- Effects: Organ dysfunction, ROS, (?) Invasive fungi.
- Liver accumulates iron but most significant sequelae are cardiac and endocrine.
- Screen by ferritin, but confirm by MRI (has replaced LIC).
- Accumulating data showing “associations” w worse prognosis.
- Rx: Phlebotomy once no longer anemic. Chelation is controversial and toxic but one study showed benefit by reducing relapse (!).
**LIC threshold** (mg Fe/g dry weight)

**Clinical relevance**
1. Sensitivity
2. Specificity

<table>
<thead>
<tr>
<th>Threshold</th>
<th>Clinical relevance</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.8</td>
<td>Upper 95% of normal</td>
<td>94% (86–97)</td>
<td>100% (88–100)</td>
</tr>
<tr>
<td>3.2</td>
<td>Suggested lower limit of optimal range for LICs for chelation therapy in transfusional iron overload</td>
<td>94% (85–98)</td>
<td>100% (91–100)</td>
</tr>
<tr>
<td>7.0</td>
<td>Suggested upper limit of optimal range for LICs for transfusional iron overload and threshold for increased risk of iron-induced complications</td>
<td>89% (79–95)</td>
<td>96% (86–99)</td>
</tr>
<tr>
<td>15.0</td>
<td>Threshold for greatly increased risk for cardiac disease and early death in patients with transfusional iron overload</td>
<td>85% (70–94)</td>
<td>92% (83–96)</td>
</tr>
</tbody>
</table>


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**Elevated Ferritin**
Iron overload: transfusion, dyserythropoiesis, associated genetic factors (HEF mutations)
Non iron overload etiology: inflammation (GVHD, infections, radiation), metabolic syndrome (immunosuppression), hepatitis (viral, drugs, GVHD, radiation), associated ETOH usage

**LIC predicts body iron stores, changes in LIC show changes body iron with chelation therapy, calculate iron balance, predicts risk of hepatic complications and risk of extra-hepatic complications**

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**Inflammation** → **Elevated Ferritin after HCT** → **GVHD** → **Iron overload**

**R2 MRI liver- LIC** (Ferriscan)

**Sensitivity and specificity of R2-LIC measurements to biopsy LIC**

**Iron overload** → **Therapeutic and preventive strategies:**
- Iron depletion
- Chelation post-HCT-ongoing clinical trials
- Phlebotomy- if not anemic

Blood. 2013 Aug 29;122(9):1539-41
Latency period of 3-5 yrs, incidence increases with time

- ~1-2% at 5 yrs, ~2-6% at 10 yrs, ~4-15% at >15 yrs

Risk factors for second solid cancers

- Previous exposures (HPV infection)
- Primary therapy (chemotherapy/RT)
- Conditioning regimen (TBI)
- Graft-vs-host disease

DIAGNOSIS

- Pre-HCT
- HCT
- Post-HCT

Genetic predisposition
Age & Gender
Lifestyle factors

Bone Marrow Transplant. 2013;48:363-8
Majhail et al. Bone Marrow Transplant 2012
Socié & Rizzo. Semin Hematol 2012
Clin Cancer Res. 2009;15:2219-21
Rizzo JD. Blood 2009;113:1175-83
Second malignancies in long-term survivors

- Cumulative - 11.5
  2.3% at 15 years
- Most frequent cancers
  - Skin
  - Oral cavity & larynx
  - Cervix/uterine
- Risk factors:
  - Older age
  - cGVHD

Kolb et al Ann Intern Med 1999;131:738-44
Second malignancy

Cumulative probability of developing a malignant neoplasm as a function of time after bone marrow transplantation

Kolb et al Ann Intern Med 1999;131:738-44
Second malignancies in long-term survivors

- Cumulative prob – 6.1 1.5% at 10 years
- Most frequent cancers
  - Liver cancer (HCV related)
  - Oral cavity
  - Cervical cancer
- Risk factors:
  - cervical cancer - older age
  - skin cancer - cGVHD

Most common second cancers are linked to HPV

- **Cervical cancer**
  - HPV-16, 18 cause ~70% of anogenital cancers

- **Oropharyngeal squamous cell cancer**
  - > 5000 cases, 35.6% HPV+ (Kreimer et al 2005)
  - Of these, 86.7% HPV-16
  - HPV-16 in 72% of cases (D’Souza et al NEJM 2007)
  - HPV-16 precedes cancer by 10 years (Mork et al NEJM 2001)

- **Skin cancer**
  - HPV in 70-90% cutaneous SCC (Dermatol Surg 2004)
  - HPV SCC in renal transplant- 3 drugs > 2 IMS

Socié & Rizzo. Semin Hematol 2012
Rizzo JD. Blood 2009;113:1175-83
35 (92.1%) had cervical cytology
  ▪ 3 less than 18 years
Abnormal cervical cytology - 14 (40%)
  ▪ 12 (34%) with HPV squamous intraepithelial lesions
    - High grade 8 (23%)
    - Low grade 4 (11%)
  ▪ 2 ASCUS and HPV high/low risk subtype negative
Median time to abnormal: 51 months (range 17-153)
Median age: 42 years (range 19-62)
  ▪ Only 3 patients < 42 year with dysplasia
HPV related cervical dysplasia

- **Factor associated with cervical dysplasia**
  - Extensive cGVHD on prolonged immunosuppressive therapy (OR 5.4, p=0.01)

![Graph showing duration of IST and cervical dysplasia](image)

Second malignancy

Pattern of risk for second malignancy after SCT

# Screening Recommendations

<table>
<thead>
<tr>
<th>Site</th>
<th>Screening recommendations*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>Mammogram annually starting age 40†; begin at 25 or 8 years after RT if chest has received ≥20 Gy</td>
</tr>
<tr>
<td>Cervix</td>
<td>PAP smear annually (for regular test) or every 2 years (for liquid based test)†</td>
</tr>
<tr>
<td>Colorectal</td>
<td>Fecal occult blood annually and/or flexible sigmoidoscopy or barium enema every 5 years or colonoscopy every 10 years starting age 50†</td>
</tr>
<tr>
<td>Skin</td>
<td>Yearly skin exam†</td>
</tr>
<tr>
<td>Lung</td>
<td>Yearly pulmonary exam with imaging as appropriate</td>
</tr>
<tr>
<td>Oral</td>
<td>Yearly oral cavity exam</td>
</tr>
<tr>
<td>Thyroid</td>
<td>Yearly thyroid exam</td>
</tr>
</tbody>
</table>

* Adapted from Children’s Oncology Group guidelines and EBMT/CIBMTR/ASBMT guidelines - 2012/ 2013
† Similar to American Cancer Society recommendations for general population cancer screening
10 year old with Hodgkin’s lymphoma treated with autologous HCT

60 year old with AML treated with allogeneic HCT and has GVHD

RISKS ARE NOT SAME

Screening Needs to be Individualized
HPV Vaccine Recommendations
- The quadrivalent HPV vaccine is approved for males and females aged 9-26 years to prevent HPV-related diseases including cervical, vulvar, and vaginal cancers and precancers in females, as well as anal cancers and precancers and genital warts in both females and males.

- We recommend vaccination starting at ≥12 months post-transplantation, regardless of prior sexual activity and exposure to carcinogenic strains.
Psycho-social Issues long-term survivors

  - ↑ depression, sleep and sexual problems (p<0.001, <0.01, <0.01)
  - Depression (OR 3.5)
  - Less likely to receive MHT, social support, dyadic satisfaction, spiritual well-being, more loneliness than survivors and controls

- Sleep quality *(Annals of Behavioral Medicine 2009)*
  - 45% with significant impairment in sleep
  - Sleep quality was significantly associated with severity of cGVHD
Psycho-social Issues long-term survivors

- Psychosocial (PS) adjustment
  *(Biol Blood Marrow Transplant 2009)*
  - $N=120$; median follow-up 5 years (range 3-15)
  - 29 (24%) survivors with poor adjustment
  - Unmarried and greater physical symptoms predicted poor PS
  - Poor PS adjustment associated with poor HRQL

- Spiritual well-being (SpWB) *(Journal of Psychosocial Oncology 2009)*
  - $N=98$; median follow-up 4 years (range 3-14)
  - Functional Assessment of Chronic Illness Therapy–General & Spiritual
  - SpWB contributed to strength and resiliency in managing the challenges of recovery and HRQL
  - Implications: Identify survivors at risk for poor SpWB and to identify interventions and resources that may enhance SpWB
HR QOL

• Discordance between actual and anticipated diminution in QOL is cause of great dissatisfaction.
• Greatest decline immediately after HSCT with gradual recovery.
• Physical recovery precedes fatigue, dyspnea, sleep or sexual.
• 19% recovered on all outcomes at 1 year and 63% by 5 years.
• 50% return to work at 1 year and 84% by 5.
• Beyond 5 years, most survivors are disease free with excellent performance.

Mental Health

#1. Neurocognitive deficits in 40% (TBI dose related, and perhaps TNF)
#2. Depression in 1/3
#3. PTSD 5%.

------------------------

• Rx: exercise, behavioral intervention, counseling, meds.
Patient-reported symptoms at 10 years

**MOST PREVALENT**

- tiredness (90.9%), lack of energy, sore muscles and difficulty concentrating (69.7%), nervousness, tension (66.7%) decreased sexual interest, difficulty sleeping (60.6%).

**MOST DISTRESSING**

- Tiredness
- Decreased sexual interest
- Muscle soreness

Survivors experiencing more symptom distress had lower HRQOL ($p<0.001$)

Courtesy Margaret Bevans - NIH
Collaborative research

- High Dose Influenza Vaccine Compared to Standard Dose in Allo-SCT Recipients
- Personalized care plans for hematopoietic cell transplant survivors
- Chronic GVHD studies
- Registry studies (CIBMTR)
- BMT-CTN (SOSS)
Conclusion

- The number of post stem cell transplant survivors is increasing and they deserve life-long surveillance and research
- Most late effects are linked to chronic GVHD
- Late complications account for significant morbidity and late mortality but many will have excellent QOL
- Role of transplant team - identify issues and coordinate care with the referring physician
- An understanding of the late effects of SCT will allow effective prevention or management of transplant related problems
Late effects resources
How do we handle all these issues....?

- Building a transplantation physician workforce for growing need
- Recruitment starts during residency/ house-staff

Please spread the word...
Is BMT at an evolutionary dead end?
“Looks like you’re going to live to a ripe old age.”