The Dual Diagnosis of Diabetes and Cancer
WADE 2018

Line Goulet RN, BSN, MEd, CDE
Erin Simms RDN, CNSC, CDE

2009 ACS, ADA, EAS Study of Diabetes, ECO

Cancer pts with Diabetes
- No guidelines for BG control
- Worse outcomes R/T
  - Reduced Quality of Life
  - Increased mortality
  - Reduced survival
  - Increased infection rates
  - Higher cardiometabolic risk

Diabetes and Cancer
A Consensus Report
Diabetes Care 33:1674-1685, 2010
Worse outcomes attributed to:
- Co-morbidities R/T diabetes
- Cancer treatment- steroids, drugs ie mTOR inhibitors
  - Tx S/E diarrhea, CIPN, cardiotoxicities
- Hyperglycemia in people without diabetes
- Unmasking of DM
- Steroid induced hyperglycemia
- Short term hyperglycemia causes immunological changes and immune suppression
  - Weakened T cells ability to attack
  - Compromised neutrophils
  - Increased rate of infection
  - Increased cancer recurrence and mortality


BG > 200 mg/dl
- MD Anderson Cancer Center
  - ALL pts treated with induction therapy with high dose dexamethasone
    - 37% had hyperglycemia but only 7% had dx DM
    - Shorter median survival
    - Sepsis and infection
  - ALL children 56% hyperglycemia
  - International study 67% at some time during induction therapy
    - Increased complications and death

Safe and Effective Dosing Basal-Bolus Insulin in Patients Receiving High Dose Steroids HyperVCAD Chemotherapy. Brady et al. Diabetes Technology & Therapeutics VOL. 16, NO.12, 2014

Metabolic Syndrome and Cancer
- Adult survivors of acute leukemia in childhood have:
  - have a higher than expected frequency of obesity;
  - early mortality from cardiovascular disease;
  - evidence of insulin resistance and increased prevalence of multiple CVD risk factors;
- Childhood leukemia HCT Survivors
  - Increased risk for metabolic syndrome;
- Adult HCT survivors
  - High prevalence of MS compared to pop controls.

Our Quality Improvement Plan 2010

Recognizing that close partnership and communication between oncologist, PCP/endo, CDE with pt at center improves outcomes
Process for identification and referral of cancer pts at high risk for hyperglycemia, with or without diabetes.
Multi-disciplinary/team approach
Early evaluation & intervention: diabetes education and support, increased glucose monitoring,
Early nutritional consult for most pts with cancer
Insulin initiation and management per Policy Guidelines

Overview

• Coordination of Care
• Cancer
• Hematopoietic system
• Treatment Modalities
• Potential Side Events
• Survivorship
• Implications for practice

Survivorship

Definition: Begins at diagnosis, includes those receiving treatment, to managing cancer as a chronic disease
A Journey of Survivorship

- 65% of adults who are dx with cancer will be alive after 5yrs (75% children)
- 18.1 billion survivors in 2020
- Many aspects of care and collaboration
- Prevention, surveillance, intervention and coordination


Prevention
as part of DSME
- Promoting healthy wt and exercise to reduce risk
- Remember to make your CDE a part of your cancer team

Surveillance: Reinforce
- Mammograms
- Colon screening

Intervention
Improving outcomes
- Changing diabetes care R/T
  - Adverse events
  - Steroids
  - New dx
  - Nutritional support
  - Support
  - Coping strategies

Coordination
- Partnership
  - with PCP, oncologists, navigators, Survivorship coordinators
- Assessment of impairments
- Glucose control
Global cancer statistics

- Cancer is a leading cause of disease worldwide
- 12.7 million worldwide dx in 2008
- Rate projected to increase by 75% to 22 million cases in 2030 r/t aging, tobacco use, reproductive, dietary and hormonal risk factors

International Agency for Research on Cancer and Cancer Research 2012

Advanced Aging is most important risk factor

Risk Factors

<table>
<thead>
<tr>
<th>Aging</th>
<th>Genetic alterations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure to</td>
<td>Viruses</td>
</tr>
<tr>
<td>Chemicals carcinogens</td>
<td>HPV-cervical</td>
</tr>
<tr>
<td>Physical carcinogens</td>
<td>Hepatitis B-liver</td>
</tr>
<tr>
<td>Asbestos</td>
<td>Alcohol</td>
</tr>
<tr>
<td>Benzenes</td>
<td>Overweight and obesity</td>
</tr>
<tr>
<td>Radiation</td>
<td>-insulin resistance</td>
</tr>
<tr>
<td>Tobacco</td>
<td>Physical inactivity</td>
</tr>
<tr>
<td>Arsenic</td>
<td>Poor nutrition</td>
</tr>
<tr>
<td>Nickel</td>
<td>Decreased access to healthcare</td>
</tr>
<tr>
<td>Sunlight</td>
<td></td>
</tr>
</tbody>
</table>

National Cancer Institute
ACS Cancer Facts and Figures 2017

- 15.5 million alive 2016
- Recent diagnosis
- Receiving treatment
- Dx yrs ago with no current detected cancer
- 1,688,780 expected to be dx in 2017
- WA 35560
- OR 21780
- ID 7310
- AK 3600
- CA 176,140

ACS 2017 Leading sites of New Cancer Estimates

Men
- Prostate 19% 161,360
- Lung and bronchus 14%
- Colon and rectal 9%
- Bladder 7%
- Melanoma of skin 6%
- Kidney and renal pelvis 5%
- Non Hodgkin lymphoma 5%
- Leukemia 4%
- Oral and pharynx 4%
- Liver and bile duct 3%

Women
- Breast 30% 252,710
- Lung and bronchus 12%
- Colon and rectal 8%
- Uterine 7%
- Thyroid 5%
- Melanoma 4%
- Non Hodgkin lymphoma 4%
- Leukemia 3%
- Pancreas 3%
- Kidney and renal pelvis 3%

ACS 2017 Leading sites of death estimates

Men
- Lung and bronchus 29%
- Colon and rectal 9%
- Prostate 8%
- Pancreas 7%
- Liver and bile duct 6%
- Leukemia 4%
- Esophagus 4%
- Bladder 4%
- Non Hodgkin lymphoma 4%
- Brain & other nervous system 3%

Women
- Lung and bronchus 25%
- Breast 14%
- Colon and rectal 8%
- Pancreas 7%
- Ovary 5%
- Uterine 4%
- Leukemia 4%
- Liver and bile duct 3%
- Non Hodgkin lymphoma 3%
- Brain & other nervous system 3%
Overweight and obesity associated with different types cancer

- Adenocarcinoma of esophagus
- Breast cancer in menopausal women
- Colon and rectal
- Endometrium
- Gallbladder
- Gastric/cardia
- Kidney
- Prostate
- Liver
- Ovary
- Pancreas
- Thyroid
- Meningioma
- Multiple myeloma

2014 – 631,000 dx cancer R/T weight
55% of all cancers dx in women
24% in men

Our Process

- Referral (insurance, H&P, pathology, histology)
- Nurse navigator, financial navigator (FN)
- Consultation with oncologist
- Further testing, CT, BM bx, PET
- Plan and treatment proposal
- Pt and family education (consult request initiated with SW,RD,RNCD)
- Treatment and surveillance
- Symptom management
- Palliative and hospice care
- Survivorship Program
Sarah’s Case

- 52 yo dx with rt breast with lymph node involvement
- Lumpectomy
- ER +, PR-, HER-
- Taxotere & Cytoxan q3weeks x 4 (3 months)
- Dexamethasone 12mg IV premed
- Dexamethasone 8 mg po D0,2,3
- 5 weeks radiation
- Letrozole daily x 5 yrs or until disease progression
- DSME 4 yrs ago @ dx, Metformin 500mg BID, A1C 6.6%
- BMI 28.7

What is Cancer

Cancer is abnormal growth of cells

Rapid growth with limited space and nutrition

Some are hereditary or familial 5-10%
Most are sporadic 90%
Mutations happen in cells all the time

Our DNA repair genes recognize and repair the abnormality
If it can’t be repaired, the process begins to cause it to die
apoptosis

Mutations that occur in genes that control cell division,
check for errors or cause programmed cell death (p53 tumor
suppressor gene) lead to cancer
These mutated genes are called Oncogenes

Immune System Function

- Protect against foreign invaders
- Maintain homeostasis
- Provide surveillance
- Immune response
  - Coordinated action
  - Target invading microbes, infected cells while ignoring healthy
  cells
Mechanism of Cancer Development

- Evade checkpoint and cell signals to stop or for apoptosis
- Form blood vessels to develop source for energy and food (angiogenesis)
- Invade other tissues and spread (metastasis)
- Evade immune system and avoid destruction

Cancer Cell and Normal Cell Characteristics

<table>
<thead>
<tr>
<th>Cancer Cell</th>
<th>Normal Cell</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shape: Irregular</td>
<td>Shape: Regular</td>
</tr>
<tr>
<td>Nucleus: Larger, darker</td>
<td>Nucleus: Proportionate</td>
</tr>
<tr>
<td>Growth: Out of control</td>
<td>Growth: In control, systematic</td>
</tr>
<tr>
<td>Maturation: Immature or doesn’t mature</td>
<td>Maturation: Death-Apoptosis</td>
</tr>
<tr>
<td>Communication: None, no function</td>
<td>Communication: Function</td>
</tr>
<tr>
<td>Visibility: Invisible to immune cells</td>
<td>Visibility: Invisible to immune cells, have ID</td>
</tr>
<tr>
<td>Blood supply: Tumor angiogenesis</td>
<td>Blood supply: Angiogenesis during repair</td>
</tr>
<tr>
<td>Oxygen: doesn’t need or like</td>
<td>Oxygen: Requires oxygen</td>
</tr>
<tr>
<td>Glucose: Loves, craves glucose</td>
<td>Glucose: Requires some glucose</td>
</tr>
<tr>
<td>Preferred Nutrient: Glucose</td>
<td>Preferred Nutrient: Glucose, fat, protein</td>
</tr>
<tr>
<td>Cell environment: Acidic</td>
<td>Cell environment: Alkaline</td>
</tr>
<tr>
<td>Energy Efficiency: Very low 5%</td>
<td>Energy Efficiency: Very High 95%</td>
</tr>
</tbody>
</table>
Chronic inflammation

- Structural damage to immune cells
- Limits immune system’s ability to detect and arrest aberrant cell growth
- ↑ production of free radicals
  - Disrupts insulin signals and damages DNA
  - Pro-inflammatory cytokines IL-6, TNF promote expression of genes
    - Increased cell proliferation and angiogenesis
    - Inhibition of apoptosis

Collins, K. The Diabetes-Cancer Link, Diabetes Spectrum 27:4, 2014

Cancer and Obesity

↑ adiposity and obesity

Insulin resistance

↑ bio-available sex hormones

↑ insulin

↑ proliferation

↑ genomic instability

↓ apoptosis

Insulin Resistance

- Inhibited metabolic effect
- Increase in signal through kinase pathways that promotes cell proliferation
- Increased insulin production exaggerates activation of cell division
- Cancer cells have increased concentration of insulin receptors
- Elevated insulin increases production of IGF-1
- IGF-1 more potent in promoting cell proliferation and inhibiting apoptosis

Collins, K. The Diabetes-Cancer Link, Diabetes Spectrum 27:4, 2014
Insulin and Insulin-like Growth Factor

Cancer cells → Elevated expression of VEGF
- Insulin receptors and IGF-1 over expressed
- Stimulation of cancer proliferation and metastasis
- High glucose uptake independent insulin receptor

- angio genesis
- IGF-1 stimulates vascular smooth muscle cell proliferation and migration

GHR, IGF -1 and IR in Cancer

• Are expressed in many hematologic and solid tumors

• Associated with poor survival in breast cancer
  - 75% positive for estrogen receptor
  - Cross talk between receptors IR, IGF-1 and ER increases proliferation
  • Dual treatment tyrosine kinases inhibitor and anti estrogen therapy

Cancer Grading and Staging

Differentiation and Grading
How closely tumor cells resemble the normal cells

Staging
Extent of disease
Tumor Node Metastasis (TNM)

• T  Size & depth of invasion

• N  Lymph nodes size number and location

• M  Metastasis location

American Joint Commission on Cancer and International Cancer Control

Hematologic Malignancies

• Leukemia, Lymphoma, Multiple Myeloma
• Staged under other systems

Tumor Markers

- **Uses**
  - Screening
  - Diagnosis
  - Prognosis
  - Monitoring treatment
  - Detecting recurrence

- **Limitations**
  - Elevated in benign conditions (CEA in smokers)
  - Elevated late stage
  - Not specific
  - More than one type
Treatment Approaches

Neoadjuvant
One or more modalities before the primary tx
Chemo before surgery to shrink tumor

Adjuvant
Targets minimal disease or micrometastatic high risk for recurrence
Chemo or radiation after surgery

Conditioning or preparation
Chemo with radiation to eliminate disease, space in marrow for stem cell transplant

Immunosuppression
Chemo to blunt immune response to prevent rejection allogenic SCT

ECOG Performance Status
Developed by the Eastern Cooperative Oncology Group

<table>
<thead>
<tr>
<th>Grade</th>
<th>ECOG Performance Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Fully active, able to carry on all predisease performance without restriction</td>
</tr>
<tr>
<td>1</td>
<td>Restricted in physically strenuous activity but ambulatory and able to carry out work of light or sedentary nature eg light house work, office work</td>
</tr>
<tr>
<td>2</td>
<td>Ambulatory and capable of all self care but unable to carry out any work activities; up and about more than 50% of walking hours</td>
</tr>
<tr>
<td>3</td>
<td>Capable of limited self care; confined to bed or chair more than 50% of walking hours</td>
</tr>
<tr>
<td>4</td>
<td>Completely disabled; cannot carry on any self care; totally confined to bed or chair</td>
</tr>
<tr>
<td>5</td>
<td>Dead</td>
</tr>
</tbody>
</table>

Cancer Treatment Modalities

- **Surgery**
  - Precise & local
  - Remove all or portion
  - Obtain specimens for cytopathology
  - May be only tx needed
  - Precede or follow other treatments
  - Alleviate or lessen symptoms

- **Staging**
  - Tumor markers and genetic testing
  - Immunophenotyping
    - Identifies cells based on antigen present on cell surface
  - To prevent /reduce risk
    - Familial breast cancer

Radiation

- Local, specific target
- Follow sx to prevent recurrence
- After chemo because of permanent bone marrow damage
- Combined with chemo
- Radioimmunotherapy
  - Radioisotope & monoclonal antibody

Toxicities

- Skin
- Lung
- Heart
- Functional-swallowing
- Pain
- Fatigue

Chemotherapy

- Systemic
- Single or combination agents
- Limited by toxic effects on normal tissues
- Tumorcidal effect in hormone sensitive tumors
- Specific sequence to maximize response and minimize side effects

- Based on cellular kinetics
  - Cell cycle
  - Cell time
Cell Cycle Specificity

Cell Cycle Specific
- Effect specific part of cycle
- Given in cycles, divided doses or continuously
- Most effective when given on regular treatment schedule

Non cell cycle specific
- Effects on all phases even G0
- Cell kill proportional to amount drug
- Dose dependent- can delay treatment so higher dose given

Cell time and growth fraction
- Short cell cycle
  ↑ cell kill
- Continuous infusion of cell cycle specific
  ↑ cell kill
Cells that divide frequently- epithelial cells, embryonic cells, blood stem cells and cancer cells
↑ % of cells dividing at a time- ↑ cell kill by cycle specific
↓ % - ↑ sensitivity to non cycle specific

Administration
- Oral
- IM
- Subq
- IV
- IA
- Intra peritoneal
- Intrathecal
- Intrapleural
- Intravesicular
- Interventional radiology
- Surgery
Treatment

- Cycles
- Weekly, q2w q3w
- Day 1,2,3,4,5
- Supportive tx R/T AE
  - Hydration, GCSF
- Monitor blood counts:
  HCT, neutrophils, platelets, liver and kidney function, LDH
- Monitoring cancer markers
- Premeds
- Double checks
- PPE
- Increasing oral chemo
- Peripheral IV
- Venous access devices
  - Ports
  - PICCS

Side Effects

- Nausea, vomiting, alopecia, electrolyte imbalance, hand foot syndrome
- Myelosuppression most common dose limiting toxicity
- GI mucositis, anorexia diarrhea, constipation
- Fatigue
- Edema
- Tumor lysis syndrome
- Cardiotoxicity (lifetime cumulative dose limits with anthracyclines)
- nephotoxicity
- Pulmonary toxicity and fibrosis
- Radiation recall
- Photosensitivity
- SE r/t infusion
- Secondary malignancies

Implantable Devices

- Implanted subcutaneously instead of patient having a port outside of body
  - Medport and Portafts are the most common
  - No dressing is required
  - Accessed by a thinner needle
  - More expensive
Hormonal Therapy

- Treat cancer
- Ease symptoms
- Oral
- Injectable
- Surgery

- Breast
- Prostate
- Neuroendocrine tumors
  - Sandostatin q4w
    - Inhibits secretion of insulin and glucagon
    - Severe hypoglycemia
    - Hyperglycemia in Type2 and PWO DM
    - Tx sulfonylurea induced hypoglycemia

Biotherapies and targeted agents

- Systemic
  - Mimic or impact signaling pathways to control cellular function
  - Target mutations
  - Modify immune defenses
  - Specific to target single receptor on surface or enzyme within
  - In or outside cell

- Prevent spread
- Help repair
  - Vaccines
  - Interleukins
  - Interferons
  - Colony stimulating factors
  - Monoclonal antibodies

Cell Communication

Cell communication through chemical signals
- Hormones, growth factor, ligands (insulin)
  which trigger biochemical chain of events
- Tyrosine kinase (90 types) receptors
- Receptor Non tyrosine cytokines
Monoclonal antibodies

• Capacity to act as an antibody by target specific antigen

CD38, CD18, CD19

CD – cluster of differentiation
Cell surface molecules of leucocytes that are distinguishable by monoclonal antibodies as immunological marker

Monoclonal antibodies

• Rituximab
  – CD20 B lymphocytes
  – Binds to the receptors and recruits NK

• Bevacizumab
  – Targets vascular endothelial growth factor (VEGF)
  – Prevents VEGF from binding to and inhibits new vessel growth
Sample order
B cell lymphoma

- D1 Rituximab
- D1-4 Etoposide, doxorubicin, vincristine
- D5 Cyclophosphamide
- D1-5 Prednisone 60 mg/m2 BID
- D6 GCSF 5 mcg/kg
- Q3W x 6

Some Side effects

- Flu like symptoms
- Rash
- N&V
- Swelling
- Tumor lysis syndrome
- Progressive multifocal leukoencephalopathy

Tyrosine Kinase Receptors

- Multiple types of cell surface receptors for various hormones, cytokines and growth factors
  - EGFR, IR, IGL-1
- Involved in cellular signaling pathways and regulate key cell functions - proliferation, differentiation, anti-apoptotic signaling
- Mutated in cancer – unregulated growth
Targeted Therapy
EGFR family of TKR
- EGFR
- HER-2

Over expressed in some breast cancers and acts as major signaling partner for other EGFR members

Tyrosine Kinase Receptors
Major Concepts
- Receptor tyrosine kinases control cell metabolism and proliferation
  - Growth factor signaling through Ras
  - Mutated cell signaling genes in cancer cells are called oncogenes
  - Insulin signaling through PI-3 kinase
- TNF receptors activate protein complexes that induce cell death and survival

Side Effects TKI, mTOR
- Depends on cellular pathway being disrupted
- Drug specific
- Hypersensitivity common
- Severe dermatological toxicities
- Cardiac dysfunction: edema, cardiomyopathy, ↓LVEF, QT
- Hepatotoxicities
- N&V
- HT
- fatigue
- ↑BG (mTOR)
- Chronic or long term Rx
Cancer Immunotherapy

- Prevent bypass of normal immune checkpoints
- Use our immune system as a network
- Checkpoint inhibitors
  - Remove disguise and flag them for destruction by activated T cells

The pluripotent stem cell

Cytokines

- Proteins produced by WBC
- Work as chemical messengers
- Regulate nature and intensity of immune response
Checkpoint Inhibitors

- Ipilimumab (Yervoy®)
  - CTLA-4
- Nivolumab (Opdivo®)
  - PD-1
- Pembrolizumab (Keytruda®)
  - PD-1
- Atezolizumab (Tecentriq®)
  - PD-L1
- Melanoma
- NSCLC, melanoma, renal cell carcinoma, Hodgkin lymphoma
- NSCLC, melanoma, Squamous cell of head and neck
- Bladder cancer, NSCLC
- Frequency of dosing?

This is how the new immunotherapy for cancer works

1. Normal work of the immune system
2. Dampening of T-cells
3. Actions of the new inhibitor drugs
4. Result of immunotherapy

---

frequency of dosing?
Implications for Practice
Immune-related adverse events

- Focused assessments
  - Thyroid panel
  - Pituitary function test
  - Liver function test
  - Pancreatic enzymes
  - Physical, psychiatric

Pt education, wallet card

Early recognition

Early treatment with steroids at grade 1 or 2

- Exacerbation of inflammatory response cause by immune system

- More common: Fatigue, colitis, pneumonitis, dermatitis, hepatitis

- Rash, pancreatitis, endocrinopathies

Checkpoint Inhibitors AE

- 7-18 weeks after start of treatment (22+ months)
- Colitis/diarrhea most common
- Grade 1 - Clinical or diagnostic, increase of less than 4 stools/day over baseline
- Grade 2 – abdominal pain, mucus or blood in stool or increase of 4-6 stools/day over baseline→ corticosteroids 1mg/kg for 4-6 weeks
- Grade 3-4 → corticosteroids 2mg/kg; IV?

Chimeric Antigen Receptor (CAR) T-Cell Therapy

- Genetically modified T/NK to express CAR which binds to cancer cell
- Tumor specific antigen recognition ie CD19 on ALL cells
Sarah’s Case

- 52 yo dx with rt breast with lymph node involvement
- Lumpectomy
- ER +, PR -, HER -
- Taxotere & Cytoxan q3weeks x 4 (3 months)
- Dexamethasone 12mg IV premed
- Dexamethasone 8 mg po D0,2,3
- 5 weeks radiation
- Letrozole daily x 5 yrs or until disease progression
- DSME 4 yrs ago @ dx, Metformin 500mg BID, A1C 6.6%
- BMI 28.7

Steroids

DEXAMETHASONE
- CINV - immediate and delayed
  - Mechanism
  - Prevent infusion reaction
    - IV 12-20 mg day of rx
- Anti-inflammatory effect
  - brain mets 4-8 mg/day

Prednisone
- Multiple myeloma 60mg/m2/day D1-4
- Immunotherapy
  - 1-2 mg/kg grade 1-2
  - 2-4mg/kg grade 3-4

Causes lysis of lymphoid cells – lymphatic leukemia, myeloma, malignant lymphoma
DEX 20-40 mg/day
D1-4,9,12,17-20, repeat every 28 days
Recruits malignant cells out of G0 phase (cell phase specific rx)
Improve appetite
Acute Stage
- Diagnosis, staging and treatment decisions
- Acute and potential losses
- Disruption in family and social roles
- Financial toxicities
- Acute side effects
- Fear of death


Extended Stage
- Completion of intensive treatment
- Possible remission
- Periodic examinations
- Intermittent therapy
- Possible terminal
- Ambiguous feelings above being alive, uncertainty of treatment or pending death

Permanent Stage
- Cure
- Extended or long term survival
- Late effects of disease and therapy
- Workplace discrimination and insurance issues
- Health promotion
- Disease prevention
- Improving QOL
- Cancer Survivorship Plan
  - Type of cancer
  - Treatment
  - Potential side effects
  - Recommendations for follow up

Morgan 2009
Psychosocial and Spiritual Assessment

• Influence of culture, spirituality, gender, sexual preference, age & healthcare
• Psychosocial components
• Altered body image
• Reproductive and sexual health
• Emotional state
  – Depression, anxiety, fear of recurrence, family conflict, survivorship guilt

Psychosocial and Spiritual Assessment

• Socioeconomic considerations R/T screening, dx, treatment, and FU
• Coping strategies
• Stress response and crisis management
• Psychosocial assessment
  – Spiritual, sexual, distress, coping, family function, relationship role changes and QOL
• Communication strategies

• I’ve been managing this for 20 years
• I need protein
• I’m not eating as much so I don’t check
• I don’t have extra strips
• My A1C was OK
• I don’t have time
• I’m too tired
• Education in our programs- reducing risks
• Maintaining our relationships- PWD and PCP
• Addressing beliefs and barriers – nutrition consult
• Managing of steroid induced hyperglycemia
Assessment

- BG targets, A1C, meter, prescriptions
- Meds: when they take them, consistency, S/E
- Nutrition
- Comorbidities: CVD, renal insufficiency, peripheral neuropathy, gastroparesis
- Fall risk
- Hypoglycemia risk
- Cognitive
- Support systems

Improving Clinical Outcomes

- Exercise during and after treatment: improves fatigue and recurrence by 40% in breast cancer
  - Anemia
  - Physical changes
  - Pain
  - SE
  - Surgery

Team based care, coordination, referrals, education and support

Toxicity Grading Criteria for Cancer Treatment

<table>
<thead>
<tr>
<th>Hypoglycemia</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting Glucose</td>
<td>ULN-160</td>
<td>160-250</td>
<td>250-500</td>
<td>&gt;500</td>
</tr>
<tr>
<td>No intervention</td>
<td>Change in daily management from baseline; OHA initiated; Workup for diabetes</td>
<td>Insulin therapy initiated, hospitalization indicated</td>
<td>Life threatening, urgent intervention</td>
<td></td>
</tr>
</tbody>
</table>

US Department of Health and Human Services: Common Terminology Criteria for Adverse Events Updated Nov 2017
Early monitoring/intervention

Referred to CDE before tx start
DM Med options when there are
AE from tx
When to monitor? FBG, ac, 2 hr pc dinner and HS on days of
dexamethasone
Frequent contact- q3-4 days , weekly
Sarah’s BG FBG 160-230
posted dinner 400’s

Lantus and dinner Novolog ordered by oncologist
Notified PCP, extra strips, copy of plan and progress
Checked in with pt 2-3 days
Off insulin 6 weeks after chemo.
Required GSCF for neutropenia,
hydration, wt loss R/T mucositis,
Hand foot syndrome
Port removed after radiation

• 2 yrs later recurrence in Lt breast
• ER+ PR+, HER2-
• Bilateral mastectomy
• MUGA, echocardiogram
• Dose dense Adriamycin/Cytoxin (A/C)
• Q2w x 4 doses
• Taxol q week x 12
• Anastrozole po
• Yearly FU
• Required transfusion
Case Study

George has had Type 2 diabetes x 8 years. DSME at Dx, BMI 32.4

On Metformin 500mg BID/WM A1C 7%; now 9.2%, wt loss 40 lbs since start of treatment

Dx with rectal adenocarcinoma.
RLQ ileostomy.
Oxaliplatin, 5 FU pump, Avastin, Q2w, 12 cycles (6 months)

Dexamethasone 8 mg po day before, 1, 2, 3, 4,
IV dexamethasone 20 mg day 1

Pt reported BG gradually increasing at each visit. Had not seen his PCP since start of treatment.

ED visit for BG over 500, given dose of subq insulin, IV hydration, sent home with instruction to see PCP ASAP

Effect of Steroids

- Increased hepatic glucose production
  - Gluconeogenesis (amino acids) and glycogenolysis (glycogen)
- Inhibition glucose uptake by muscle and fat
- Decreased insulin production and secretion

Results in increase in post prandial glucose 8 -12 hrs after taking med rather than increased in FBG

Consider SBGM in non diabetic pts, 2 hrs post lunch 1-2x week

Options with steroids

Prednisone
- Second generation sulfonylurea, titrate q 48-72, B/Gx 2-250 then
- ½ unit NPH per 2mg
- Peak effect on BG in afternoon
- Readjust but 10-20% based on ac dinner /HS BG every few days
- BG checks ac, HS until pattern and dose established, then ac B,D,HS

Dexamethasone
- Effect over 24 hrs
- Consider sulfonylurea
- 0.3 -0.5 units/kg
- May need basal/bolus
- Different ratio “chemo” days
- Duration may last weeks after D/C
- Withdrawal symptoms muscle pain and cramping
- QID testing
• Saw PCP the next day who increased Metformin to 1000mg BID
• Return visit to ED for BG over 500 and dehydration
• Referral from ED; contacted pt who found a new PCP who was sending him to me
• Pt prescribed insulin by new PCP
• Basal/bolus/correction, “chemo days dosing”
• Ac BG 110-142.
• Return oral agent 2 months after stop of steroids

Where do you fit in?
What can we do different as a group?

<table>
<thead>
<tr>
<th>Glucocorticoid Potency</th>
<th>Duration ½ Life Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocortisone</td>
<td>8</td>
</tr>
<tr>
<td>Cortisone</td>
<td>Oral 8, IM 18+</td>
</tr>
<tr>
<td>Prednisone</td>
<td>16-36 (peak 8-12h)</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>16-36</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>18-40</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>36-54</td>
</tr>
</tbody>
</table>

Dexamethasone 40 mg plus 20 mg IV day of infusion
Decadron aka DEX

**Side Effects**
- Gastric irritation, decreased carbohydrate metabolism, hyperglycemia, sodium and water retention, alterations in fluid and electrolyte balance, steroid induced immunosuppression, injury from rapid withdrawal, cushingoid changes, cataracts, glaucoma, ocular infections, affective behavioral changes, musculoskeletal changes.

**Prevention CINV**
- Prevent reaction

**Treatment leukemia and lymphoma**

**Brain mets**
- Inhibit prostaglandin
- Inhibits stimulation N & V
- Decreased inflammation

---

**Report Therapy Related Symptoms**

**Fatigue**
- Feeling sluggish 68%
- Depression 28%
- Difficulty concentrating 38%
- Difficulty sleeping 43%
- SOB 36%
- Pain 46%
- Numbness toes, fingers 43%
- Skin changes 25%

**Eating**
- Taste changes 53%
- Loss of appetite 44%
- Weight loss 41%
- Difficulty swallowing 30%
- Sore mouth 22%
- Nausea 51%
- Vomiting 23%
- Constipation 45%

---

**Late and long-term side effects from chemo**
- Chemobrain
- Digestion problems
- Bone, joint, soft tissue problems
- Endocrine system problems
- Emotional difficulties
- Lung toxicities
- Lymphedema

- Fatigue
- Cardio toxicities
- Peripheral neuropathy
- Secondary cancers
- Other
CINV

- Nausea and vomiting common
- Impact QOL and often underestimated
- Prevention
- Guidelines for prevention and treatment
  – ASCO, NCCN, ONS PEP

Acute vs delayed; High vs Moderate vs Low
Oral, breakthrough, anticipatory

CIPN

- Related to cumulative dose
- Infusion duration
- Individual risk factors influence development and severity of neurotoxicity
- Preassessment
- Assessment at each visit
- Dose reduction
- Discontinuation
- Acupuncture
- Physical activity
- Massage
- Cold therapy
Glutamine

- Amino acid
- Most prevalent in body
- Essential for skeletal muscle function, immune, nervous and digestive systems
- Powder 10-15gms BID, 7-14 days, repeat with each cycle

Therapeutic use
- Reduce and prevent neuropathy associated with taxane and platin based chemo
- Prevent taste changes, mucositis, esophagitis

Lawenda, B; Use Glutamine to Reduce severity of Mucositis and Neuropathy during Chemotherapy or Radiation, Integrative Oncology Essentials, Feb 25, 2013

Increased Cardiovascular Risk
US National Cancer Institute
- 13.7 Million cancer survivors alive in 2012

- Overall survival
  - 67% of adults at 5 y
  - 75% of children at 10 y
  - Increased risk of CV events

Delhaye 2008, 20, pp 997-998
Perreault 2011, 155, pp 103-110
The landscape: Increase in Cardiovascular Risk

 Anthracyclines and Types of Cardiovascular Toxicities

**Acute** occurring with onset of clinical manifestations within 2 weeks from end of treatment

**Early-onset chronic** within 1 year. The most frequent form of cardiotoxicity, usually presenting as DCM leading to HF

**Late-onset chronic**, developing years to decades after end of chemotherapy
Cardiovascular Complications from Cancer Treatment

Chemotherapy
- Cardiomyopathy
- Asymptomatic
- Arrhythmias
- Coronary heart disease
- Hypertension

Radiation
- Coronary heart disease
- Valvular heart disease
- Pericardial disease
- Vascular disease
- Congestive heart failure
- Arrhythmias

Medical Nutrition Therapy for Blood Glucose Control in Cancer Patients
Erin Simms, RDN, CD, CNSC, CDE
Certified Diabetes Educator
WhidbeyHealth Medical Center
Coupeville, WA

Glucocorticosteroids
- Why used in cancer treatment
  - Treat and prevent nausea
  - Inflammation reducer
    - Brain metastasis
  - Reduce hypersensitivity to treatment
  - Appetite stimulant
  - Pain reducer
GLUCOCORTICOSTEROIDS

- Impacts glucose metabolism
  - Increased insulin resistance due to "down regulation of GLUT-4" in the muscle
  - More insulin needed for the uptake of glucose into the cell
  - Postprandial hyperglycemia
  - Promotes glucose production in the liver
  - Decrease insulin release from the islet cells

IMPACT OF IMPAIRED BLOOD GLUCOSE CONTROL

- Dehydration
- Infection
- Surgical Complications
- Catabolic weight loss
- Reduced treatment eligibility
- Hyperosmolar Non-Ketotic state (HNK) – rare
- Diabetic Ketoacidosis (DKA) - rare


NUTRITION THERAPY

- Meet with patients to review current oral intake
  - Evaluate impact of cancer treatment on oral food and beverage intake
    - Chemotherapy, XRT, surgery...
      - Nausea/vomiting
      - Taste alterations
      - Anorexia
      - Weight gain/loss
      - Diarrhea/constipation
      - Wound healing
NUTRITION THERAPY

- Encourage hydration if hyperglycemia
  - Low Carbohydrate Fluids
    - water flavored: flat or carbonated with lemon, lime, mint…
    - dilute Gatorade or G2
    - coconut water (11 oz = 15 grams carbs but also get K+)
    - almond milk: original (8 grams carbs or low sugar 4 grams per 8 oz)
    - herbal teas
    - NUUN (electrolyte tablets mix in 16 oz water)

Table 1
Preparations of Glucocorticosteroids

<table>
<thead>
<tr>
<th>PREPARATION</th>
<th>GLUCOCORTICOID POTENCY</th>
<th>MINERALOCORTICOID EFFECT</th>
<th>HALF-LIFE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortisone</td>
<td>1.0</td>
<td>++</td>
<td>4-6 h</td>
</tr>
<tr>
<td>Prednisone</td>
<td>4.0</td>
<td>+</td>
<td>6-12 h</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>48.0</td>
<td>+/-</td>
<td>6-12 h</td>
</tr>
<tr>
<td>Desamethasone</td>
<td>20.0</td>
<td>0</td>
<td>1-2 d</td>
</tr>
</tbody>
</table>

NUTRITION THERAPY

- Evaluate glucocorticosteroid dosing: amount and time
  - One time
  - Daily
  - Multiple times a day

NUTRITION THERAPY

- Discuss changes to carbohydrate load
  - Review or instruct on carbohydrate guidelines
  - Include carbohydrate information for current foods tolerating

- Educate significant others or caregivers
  - Provide written handouts

- Involve oncologist, CDE RN, others to evaluate insulin therapy if continued hyperglycemia
  - Reminder patient and family about tapering insulin if tapering steroids
OTHER CONSIDERATIONS

- Evaluate how long steroid use
- Supplement with Vitamin D3 and calcium
- Long term use lead to bone loss even short term (~ 30 days)
- Best if can get Vitamin D level checked in the blood
- Supplement based on labs
- Upper Tolerable limit of D3 is 4000 IU
- Calcium 500 mg one to two times a day (evaluate diet other supplements)

TIPS FOR EATING

Healthy Snacks = Protein + Carbohydrate

<table>
<thead>
<tr>
<th>Protein</th>
<th>Carbohydrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 oz Greek Yogurt</td>
<td>½ c Berries or Canned Fruit</td>
</tr>
<tr>
<td>1-2 TBSP Peanut/Nut Butter</td>
<td>½ c 1 whole Apple (skinned)</td>
</tr>
<tr>
<td>½ c Cottage Cheese</td>
<td>½ - 1 whole Sliced Pear or Peach</td>
</tr>
<tr>
<td>1 oz String Cheese or ½ avocado</td>
<td>5-6 Rye or whole wheat crackers</td>
</tr>
<tr>
<td>1/3 c Tuna Salad/Egg Salad, Chicken Salad</td>
<td>1 half a sandwich, pita bread, or crackers</td>
</tr>
<tr>
<td>¼ c ~ ½ c Hummus Dip</td>
<td>Raw vegetables</td>
</tr>
<tr>
<td>½ c Split Pea, Senn of Minestrone Soup</td>
<td>1 slice Multigrain Bread/Toast</td>
</tr>
<tr>
<td>½ c Vegetarian Refried Beans/Salsa</td>
<td>12 Tortilla Chips or 1 6” tortilla</td>
</tr>
<tr>
<td>1 c Soy M'k</td>
<td>Fruit (1/2 of what is together in a smoothie)</td>
</tr>
<tr>
<td>½ c Sunflower Seeds, Nuts</td>
<td>2 TBSP Tost Fruit</td>
</tr>
<tr>
<td>1-2 oz Meat, fish, poultry</td>
<td>1 slice whole grain bread</td>
</tr>
</tbody>
</table>

MORE IDEAS

- Smoothie Add ins
  - ½ to 1 TBSP Chia seeds for soluble fiber and omega 3 fatty acids
  - Flax seed meal for lignans (plant estrogen and antioxidants), soluble fiber and omega 3
  - Greek yogurt or kefir for probiotics
  - Protein powders for added protein. Aim for 10-20 grams protein per smoothie
  - Spinach adds phytonutrients (plant compounds-antioxidants) without changing the flavor. Use ½ to 1 c raw spinach leaves.
  - Avocado for extra calories and omega 3
  - Hemp seeds for protein
  - Spices-cinnamon, cayenne
  - Spirulina provide anti-inflammatory properties
  - Ice cream for added calories

- Protein foods
  - Beef, fish, poultry, pork 1 oz = 7 grams...3 oz = 21 grams
  - Tofu ½ c = 10 grams
  - Cottage cheese ½ c = 13 grams
  - Milk, soy and cow 1 cup = 8 grams
  - Veggie burger 1 patty = varies per brand 11 grams to 19 grams
  - Greek yogurt, 6 oz = varies per brand 12-18 grams
  - Peanut Butter 2 TBSP = 8 grams
  - Cheese 1 oz = 5.7 grams
  - Beans (entilis, black beans...) ½ c = 7 grams
  - Tuna 3 oz = 17 grams
  - Egg 1 = 8 grams
Thank you!

Erin Simms, RDN CD, CNSC, CDE
WhidbeyHealth Medical Center
Coupeville, WA

Lost in Transition

Resources

goulel@whidbeyhealth.org  360-678-7656x2661

- National Comprehensive Cancer Network  nccn.org
- Oncology Nurses Society  ons.org
- Puget Sound Oncology Nurses Society  psons.org
- Cancer Care  cancercare.org
- American Cancer Society  cancer.org
- American Society of Clinical Oncology  asco.org
- Cancer Net  cancer.net
- Livestrong.com
- Chemocare.com
- CJON.ONS.ORG
- US Department of Health and Human Services  cancer.gov
Uses a glucose analogue F-FDG
- Cancer cells have higher glucose uptake
- Still have reliable results with serum glucose levels 140-260mg/dl (Mirkour et al 2012)

General guidelines – do practice run 3 days before
- No strenuous activity for 24 hrs before
- Fast for 12 hrs before apt
- Check FBG, if too low treat and R/S apt
- Drink plain water only in 6 hrs before exam
- Preferred BG range 70-150mg/dl
- Specific instructions for oral agents and insulin types

PET scan - UW Medicine Radiology and Imaging Services PET FDG scan for Diabetic pts

IF YOU EVER FIND YOURSELF DOUBTING HOW FAR YOU CAN GO, JUST REMEMBER HOW FAR YOU HAVE COME
- AUTHOR UNKNOWN