Complementary and Alternative Medicine (CAM)

- **Complementary** medicine is used with conventional medicine.
  - Example: Gentle yoga for strength and flexibility during cancer treatment

- **Alternative** medicine is used in place of conventional medicine.
  - Example: Taking supplements instead of undergoing conventional treatment (e.g., surgery, radiation, or chemotherapy) for cancer.

Topics

- Basics: Stats, etc.
- Biologics: Vitamin C IV, Mushrooms, etc.
- Diet: Realistic Evidence Based approach
- Underlying systemic functional issues: Gluten Sensitivity, MTHFR mutations, Phase I or II liver detox genetic abnormalities, Poor Stress Resilency
- Wellness Approaches to minimize side effects of disease and chemo: Tai Chi, Mindfulness Practices such as meditation/biofeedback, Yoga, Acupuncture
- Other ideas
- Tips on navigating CAM world
- References: Books/Online Resources/etc.

Complementary and Alternative Medicine: Benefits, Role and Risks for Bone Marrow Failure Disease Patients

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Integrative Medicine

- Integrates complementary therapies with evidence of safety and effectiveness into conventional medical treatment with goals of:
  - Optimizing health promotion
  - Preventing disease
  - Improving patient outcomes
  - Managing symptoms
  - Improving quality of life

No Financial Disclosures
Cost of CAM…

- $37 billion/year in US
- 20 million more visits to CAM professionals than primary care

What percentage of cancer patients report using CAM?

A. 25%
B. 50%
C. 75%
D. 90%

- 62% long-term Lymphoma survivors use CAM
- 73% of hospitalized cancer patients use CAM
- 44% of German Leukemia patients use CAM, with > half not disclosing to healthcare team

Levels of Evidence

- Level I - Well designed randomized controlled trials
- Level II – Prospective or retrospective non-randomized clinical trials and analyses
- Level III – Opinions of expert committees, best case series
- Level IV – Preclinical in vitro and in vivo studies, and traditional uses

Biologics

- Green Tea
- Boswellia
- Omega 3 (Fish Oil)/ Omega 6 (Flax seeds/oil)
- Medicinal Mushrooms
- Curcumin
- Melatonin
- Vitamin K2
- Vitamin C IV

Green Tea

- Levels II, III, IV - no specific MDS/AA studies but positive randomized trial for patients with CLL - Chronic Lymphocytic Leukemia
- High in bioflavonoid antioxidants
- Also contains tannins, minerals, caffeine and L-Theanine
- Induces hematologic tumor cells apoptosis in vitro
- Many studies are done on dietary intake with typical “high intake” considered to be 5 or more cups per day

Risk of hematologic malignancies was inversely associated with green tea consumption. The multivariate-adjusted hazard ratio of hematologic malignancies for 5 cups/day or more compared with less than 1 cup/day of green tea was 0.58 (95% confidence interval: 0.37, 0.89). The corresponding risk estimate was 0.52 (95% confidence interval: 0.31, 0.87) for lymphoid neoplasms and 0.76 (95% confidence interval: 0.32, 1.78) for myeloid neoplasms.

Green Tea
- Try to get organic (not organic is likely to contain high amounts of pesticides)
- If want to take supplement
  - high quality is important
  - Typical dose is one 300-500mg capsule twice daily (each containing at least 50% EGCG) (usual cost - $15-20/month)
  - Capsules are actually cheaper than drinking high quality (organic) green tea at studied doses - 5-6 cups/day

EGCG and CLL
- 2 recent Randomized Control Trials on CLL (Rai Stages 0-2)
- Polyphenon E – concentrated green tea with EGCG content 400-4000mg/day in twice daily dosing (200-2000mg)
- About 70% of patients had WBC reduction of 10% or more and about 40% 20% or more
- Dose dependent side effects were common at higher doses: nausea, rashes. Some patients had to stop high dose
  - Cancer. 2013 Jan 15;119(2):363-70
- Currently available products contain about 200mg of EGCG/capsule – at 10 capsules/day cost is about $50/month

Boswellia
- Boswellic Acid acetate – grade III, IV
- Induces differentiation and apoptosis of human leukemia lines
- Very potent anti-inflammatory
- Very low side effect profile
- Quality is important
  - Leuk Res 1999; 23;43-50

Japanese Mushrooms
- Levels I, II, III, IV – no clinical studies on MDS/AA
- Reishi – traditional chinese medicine use
- Agaricus Blazei Murrill Mushroom aka ABM
- Coriolus Versicolor aka Asian “Turkey Tai” – best evidenced
- Shiitake
- Maitake Mushrooms
- DO NOT USE WITHOUT GUIDANCE – Protocols are complicated, often include mixes of all or some of the above, often on/off regimens, quality if critical

Curcumin
- Curcumin is an active ingredient of Turmeric (Levels II, III, IV)
- Modulates inflammation by down-regulating COX2 – nature’s Motrin
- Inhibits TNF-Alpha, IL1, 2, 6, 8, and 12
- Natural part of many world diets, especially India and Thailand
- No randomized trials for MDS/AA

Induces apoptosis in human leukemia cells.
- Biochem Biophys Acta. 1996 Nov 15;1317(2):95-100

Small positive clinical trials for Pancreatic, Colon

Absorption is increased with piperine (Bioperine)
- Avoid using during Chemo: Dietary curcumin is even enough to inhibit chemotherapy-induced apoptosis through inhibition of ROS and blockade of JNK function.
- Cancer Res. 2002 Jul 1;62(13):3868-75

Typical dose - 1000mg twice daily of concentrated extract, Meriva by Thorne is a good example
Melatonin

- Levels I, II, III, IV (no specific MDS/AA trials)
- Sleep hormone, synthesized by the pineal gland
- Also appears to be a strong anti-oxidant and regulates secretion of growth hormone and gonadotrophic hormones
- Recent Meta-analysis (total of 21 randomized trials) showed 37% reduction in all cause 1 year mortality in patients with solid tumors
  - Integr Cancer Ther. 2011 Oct 21
- Usual dose 20mg at bedtime, start at nor more then 5mg and slowly increase over 3-4 weeks

Vitamin K2

- Levels I, II, III, IV – in contrast to all other supplements, has clear evidence for MDS, both clinical trials and bench research
- Does not involve in clotting, mostly in bone and muscle health
- Similarly to Vitamin D it is more of a hormone as it effects cells via variety of receptors mediated actions
- In MDS exhibited an anti-apoptotic effect on erythroid progenitors under erythropoietin depletion.
- Pilot Study
  - 72.7% (8/11) had refractory anemia with excess blasts in transformation and 50% (6/12) had post-MDS acute myelocytic leukemia.
  - K2 reduced blast cell numbers in bone marrow and/or peripheral blood in 71.4% (10/14) of those receiving other medications for MDS.
  - Patients who used oral vitamin K2 without other medications had 44.4% (4/9) hematological improvement.

Vitamin K2

- Phase II – single arm prospective trial
- Patients with MDS with refractory anemia and refractory cytopenia with multilineage dysplasia, having either low or intermediate-1 risks of the IPSS
- 1st treatment with Vitamin K2 – 45mg (menatetrenone) – 13% response rate – improvement of Anemia and Thrombocytopenia
- 2nd – Non responders from above were given Vitamin K2 plus Vitamin D3 (0.75mcg/day) – 30% response rate
- 3rd – No known side effects, combine with at least some vitamin D

Quality is critical

- 2 types:
  - Menatetrenone (MK4) – Studied, including above study, typical dose is 45mg/day
  - Thorne has good liquid product
  - Menaquinone-7 (MK7)
    - typical dose 50-150mcg/day (BioTech makes good product)
    - No clinical studies but thought to be as effective as MK-4
    - No known side effects, combine with at least some vitamin D
  - No effect on clotting, safe to take even when on Coumadin, but if patient is on Coumadin I check PT/INR 3-5 days after starting Vitamin K2
Intravenous Vitamin C

- Evidence – levels II, III, IV – no direct MDS/AA evidence
- Safe (about 1 million infusions done between 2006-2008)
  - Only known contraindication – patients with G6PD-deficiency (easy test to check) secondary to hemolysis
  - Only 6 serious complications reported (renal failure 4 cases – 1 death, hemolysis 2 cases – 1 death – pt had G6PD deficiency, and was not screened)
- Safe to combine with chemotherapy – likely to enhance chemotherapy effectiveness
- Mild chemotherapeutic agent
- Produces H2O2, normal cells capable of quickly removing peroxide
- Appears cytotoxic for a lot of cell lines (at least 10), including leukemia
- 

We have treated hundreds of patients over years - mixed results, we are about to analyze our data.
- Mostly decreased side effects of chemo, improved energy.
- Multiple cases of long term survival at our clinic and in other places
- 2 recent small positive trials both for metastatic pancreatic cancer
- But likely more studies are on the horizon

Other Supplements

- Fish Oil – anti-inflammatory, conflicting evidence for patients with cancers, seems to improve chemo induced side effects and slows down weight loss.
- Mistletoe – used a lot in Europe, conflicting data, but some positive double blind randomized studies (not for MDS/AA), we don't use it, no US experience/trials
- Vitamin D – deficiency should be corrected, my goal for all cancer patients is 40-60 ng/ml of Vitamin D 25OH
- Glutamine, Acetyl-L-Carnitine, Alpha Lipoic Acid, probiotics – supportive role during chemo therapy to minimize fatigue and prevent diarrhea
- Ginger – high dose, decent alternative to anti-nausea medications during chemo.

What to avoid/Reality Check

- Individual oral anti-oxidant vitamins: A, E, Selenium – should not be taken for long periods of time – possible harm – Level I, II, III, IV (Vitamin C IV discussed separately)
- Retail multivitamins – no good quality, possibly harmful, level II, III, IV
- Learn how to evaluate quality/claims
  - Trusted online resources
  - Consultations with Integrative and Naturopathic Physicians
- Avoid advice by clerks/sales people at vitamin shops/stores
  - no sufficient evidence base knowledge
  - evidence that such recommendations are harmful

Diets

- Plant Based Diet – Levels II, III, IV – weak positive evidence at best
- High Fiber Intake - none
- Specific Diets: - levels III, IV – conflicting
  - Macrobiotic
  - Gerson
  - Gonzales
- Sensible approach - Low animal protein, high in greens/some fruits, avoid “dirty dozen”, anti-inflammatory principles, food allergies?

Systemic Issues to Pay Attention to

- Gluten Sensitivity – increased systemic inflammation
- MTHFR mutation – inability to convert folic acid to active form of folate (5MTHF) – may lead to increased risk of DNA mutations
- Genetic Detoxification Problems – increased accumulation of toxins: heavy metals, pesticides, herbicides, other chemicals
- Poor Stress Resiliency and frank Cortisol curve abnormalities– increased systemic inflammation
Gluten Sensitivity

- Evolutionarily speaking, wheat is a recent addition to the human diet, about 10,000 years ago.
- Gluten is the storage protein of cereal grains: Wheat, rye, barley
  - Glutelin: The alcohol-soluble fraction, glutamine and proline rich protein, and poorly digestible
  - Resistant to stomach acid and proteases
- Gliadin is the primary immunogenic trigger of Celiac disease

Gluten Sensitivity

- Evidence from the US and Finland has shown a marked increase in prevalence
- 4-fold increase in the last 50 years
- Data is based on stored serum samples and reflect a true increase in the prevalence of the disease, not related to under diagnosis.
- Reason unclear: Increased gluten in wheat with agriculture, other dietary and environmental factors

Gluten Sensitivity

- Clear epidemiologic link to Cancer – Level II, III, IV no evidence for MDS or AA links
- Treatment - Gluten Free diet, often long term, combined with several supplements: 1-6 months digestive enzymes, probiotics, fish oil, zinc, glutamine.
- Blood tests are covered by most insurances, but best is to do gluten free diet for 4-6 weeks and see if there is any improvement in:
  - Intestinal symptoms
  - Cognitive Function
  - Muscle/Joint pains
  - Rashes
  - Chronic Sinusitis, Bronchitis, etc
  - Improved Sleep and energy levels
- Absence of intestinal symptoms is common and should not preclude from testing
- Gluten Free Diet is no longer “impossible” to do, but still big time ordeal!

Methylenetetrahydrofolate reductase (MTHFR)

- Enzyme encoded by MTHFR gene
- Part of larger testing strategy called SNPs
- 2 main mutation types: 677 and 1298
- Both alter enzyme function
- So what?

MTHFR C677T mutation

Aberrant DNA methylation is frequent in the myeloid malignancies, particularly myelodysplastic syndrome (MDS) and acute myelogenous leukemia (AML).
MTHFR - treatment

- Active form of folate called 5MTHF
- Cheap and easy to obtain, typical dose 1-3 mg
- Often combined with B12 (needed as cofactor for utilization of 5MTHF)
- Very high dose prescription strength medical food/medication: Deplin 7.5 or 15 mg doses available by prescription only
- More comprehensive treatment programs may include active methyl donors such as SAMe or Methionine

Detox System Defects

Poor Stress Resiliency

The Stress Response System

- Acute – Upregulates Immune system, protective function
  - Increase in IL6
  - Increase in neutrophil count
  - Stimulation of NK cells, T Lymphocytes,
- Chronic Stress – Global Decrease in Immune function

Stress Effects on Health

- Decreased wound healing
- Decreased immune function
- Decreased testosterone
- Increased insulin
- Increased post-stress levels
- Increased viral load
- Increased risk of disease
- Genomic changes
- Increased inflammation
- Increased infection, colds,
- Increased HIV progression
- Increased inflammation
- Decreased tissue response
- Increased liver disease
- Decreased health QOL
- Increased arthritic flare
- Increased illness in children
- Increased LV dysfunction
- Increased cardiac arrhythmias
- Increased cardiac ischemia
- Decreased MI
- Increased HP
- Increased clotting
- Increased inflammation
- Decreased vaccine response

Wellness Strategies

- Acupuncture: energy, cancer treatment side effects
- Energy based exercises: Tai Chi and Yoga
- Energy treatments: Reiki, Healing Touch
- Massage
- Mind Body Practices: Meditation, MBSR, Hypnosis, Biofeedback
- Spiritual approaches: finding meaning in midst of crisis, better coping strategies
Acupuncture

Levels I, II, III, IV – no specific MDS/AA, data often conflicting
- Nausea Vomiting
- Fatigue
- Insomnia
- Anxiety
- Generally safe
- Adequate training must
- Cancer experienced acupuncturist

Tai Chi

Excellent if not Ideal exercise
- Balance
- Strength
- Fatigue
- Easy to do and learn
- No need for special place
- Basics can be learned very quickly
- Find a teacher who specializes in working with patients with chronic illnesses

Yoga

- Clinical Trial
  - N = 39 pts w/ lymphoma
  - Tibetan yoga (TY) (7 wldy sessions)
  - Wait list control
  - Patients in TY group
    - Better subjective sleep quality (P < 0.02)
    - Faster sleep latency (P < 0.01)
    - Longer sleep duration (P < 0.03)
    - Less use of sleep medications (P < 0.02)
- FIND THE RIGHT TEACHER – MUST BE THERAPEUTIC YOGA CERTIFIED
- Side effects are very common and could be serious if not done under good teacher’s supervision

CranioSacral Therapy

- Osteopathic manipulation
- Very Gentle
- Some evidence for balancing Autonomic Nervous System (ANS)
- Effects very similar to massage but safer

Reiki

- Reiki is a healing practice that originated in Japan. Reiki practitioners place their hands lightly on or just above the person receiving treatment, with the goal of facilitating the person’s own healing response.
- Effective for anxiety and fatigue - Level II, III, no specific MDS/AA studies
- Easy to learn to self-administer
- At our center we offer group class to learn basics of self Reiki in evening/weekend, cost of one 2.3 hour class $75

Massage Therapy and Stress Management

- Memorial Sloan-Kettering Cancer Center
- 1,290 patients treated over 3 yr period
- Pre- and Post-therapy sx’s recorded
- Symptom Improvement
  - Pain 40%
  - Fatigue 41%
  - Anxiety 52%
  - Nausea 21%
  - Depression 31%

Slide made by Brent A. Bauer MD
Meditation and Stress Management

- Systematic Review – Meditation & Cancer Pts
  - 3 RC trials, 7 uncontrolled trials
  - Positive results
  - Mood, sleep quality, reductions in stress
  - Dose-response effect observed
  - Frequent methodological limitations identified

- MBSR – Mindfulness Stress Reduction Program - structured 8 weeks program, often covered by insurances. We have ongoing classes at our center.

Slide contributed by Brent A. Bauer MD

Online Resources

- NCCAM at NIH: basic CAM Information: [NCCAM.nih.gov](http://NCCAM.nih.gov)
- Consortium of Academic Health Centers for Integrative Medicine: [www.imconsortium.org](http://www.imconsortium.org)
- NCI subsection on CAM: [www.cancer.gov/cancertopics/pdq/cam](http://www.cancer.gov/cancertopics/pdq/cam)

Final Points

- Be guided by someone with experience and good handle on “fast moving train” of CAM research – ideal team would have MD/DO and Cancer-Train Naturopathic Doctor or experienced cancer nutritionist.
- Do everything with your Oncologist approval, make sure your CAM provider communicate with the Oncologist well.
- Whole body approach vs doing 1 CAM modality
- Life style change rather than “short term trial” – Cancer is a chronic disease, such as high Blood pressure of diabetes
- Work with your insurance company, some CAM modalities are COVERED – call your carrier and ask: “What is my copay for …”. Big time insurance coverage improvement expected in 2014
- Flexible spending accounts will cover ANY CAM modality or Supplement if prescribed by qualified provider

Spirituality

- Dr. Puchalski: Spirituality (refers to the way) people understand meaning and purpose in their lives. It can be affected by illness or loss, and it can be experienced in many ways – not just religion, but nature, arts, humanities, and rational thinking. Some say it is God, some say it is family, and some find it in nature. It’s a very personal thing for people.

Books

- [Enjoy Every Sandwich](http://example.com)
- [Leaves Falling Lonely](http://example.com)
- [Full Blood Catastrophe Living](http://example.com)

Trust Resources in Boston

- Boston University Integrative Cancer Care
  - Some services are free or covered by insurances
    - acupuncture
    - support groups
    - Integrative oncology consultations
- The Leonard P. Zakim Center for Integrative Therapies at Dana-Farber Cancer Institute
  - [http://www.dana-farber.org](http://www.dana-farber.org)
THANK YOU

4-7-8 Breath – 3 min meditation

- Inhale on 4
- Hold breath on 7
- Exhale on 8
- If this is hard remove holding part and just do inhale 4 and exhale 8
- If you are out of breath with 4 and 8 try to count to 3 and 6.
- Abdominal Breathing
- Now think about something that you love dearly