



## **Dietary Supplement use by patients**

### **Implications for Surgical and Oncology RNs**

#### Objectives of the talk:

Familiarize Nurses with:

- Prevalence and impact of dietary supplement use
- Supplements most patients are using
- Major Pharmaceutical Categories for Dietary Supplements
- Potential side effects and drug interactions
- Recommended Resources



# Growth of an Industry



Source: *Packaged Facts Inc.*



# Herb Safety

## 1994 Dietary Supplements Health and Education Act -

Vitamins, minerals, herbs = foods.



- **No Proof of Safety or efficacy needed. Proof of harm falls on the FDA, not the manufacturer.**

- FDA can't remove a vitamin & mineral supplement considered worthless or offered at high doses.

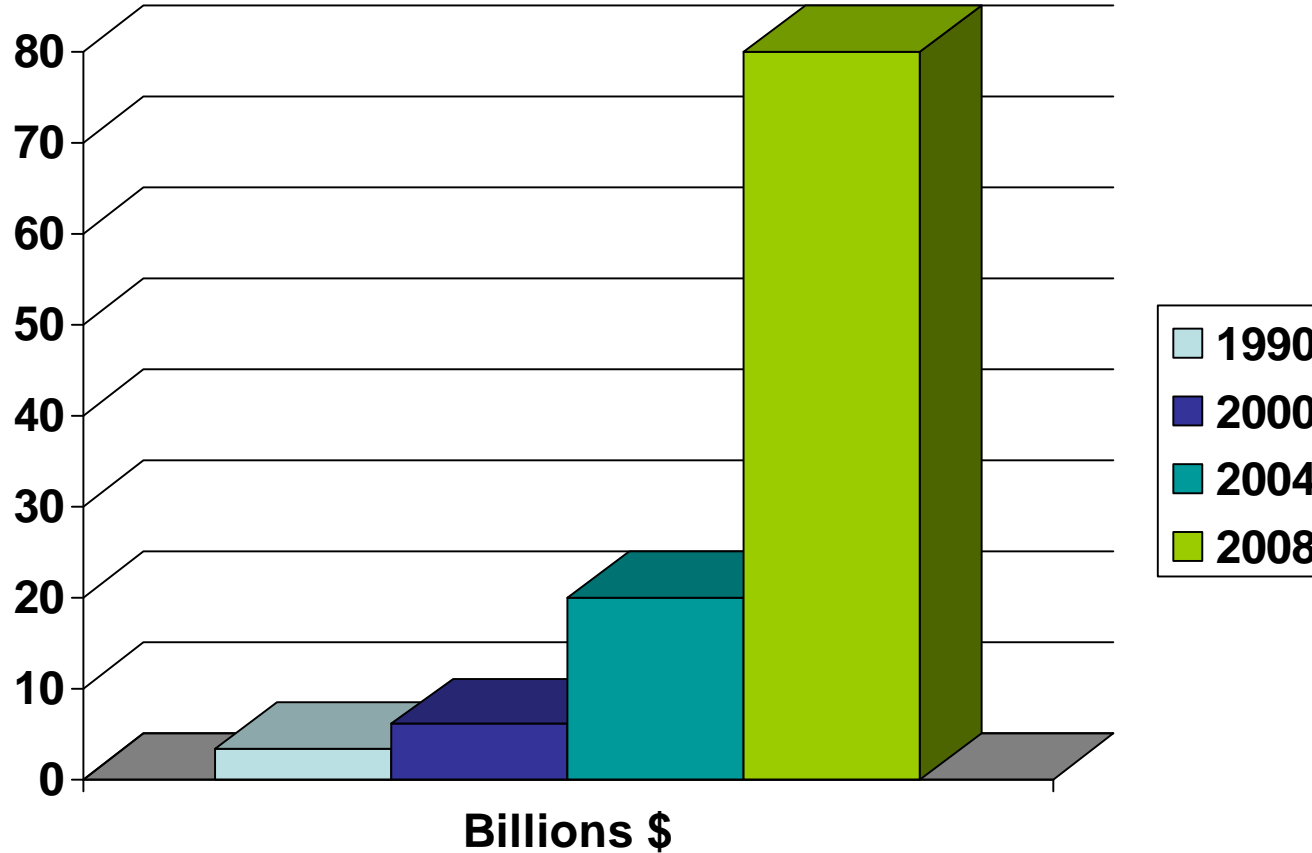
- Can only prevent packages from carrying health claims.

- Can issue alerts, warnings





# Growth in Dietary Supplement Sales





# Prevalence

## 2004 Nutraceutical Business Data:

**>158 million Americans regularly consumed dietary supplements**

**18% of users were also taking prescription medications.**

**70% do not inform their medical team of their supplement use**





# Reasons for Concern:

## Supplements instead of traditional treatment -

- Inappropriate self-diagnosis and treatment
- Delay in seeking effective medical treatment
- Financial cost of unproven therapies

## **Medical team unfamiliar w/ supplements**

- Hazardous herbs
- Potential drug interactions
- Potential to confound results of clinical drug trials





# S/E from “herbs” misattributed to study drugs



- Diarrhea, nausea, vomiting
- Hepatotoxicity
- Altered mental status
- Diuresis, edema, electrolyte disorders
- Renal failure
- Hemodynamic changes, thrombocytopenia





# Quality Concerns

- **Mis-identification**  
has led to poisonings
- **Contamination**  
fungi, bacteria, animal waste
- **Fraud**
  - **Substitution with less expensive herbs**
- **Adulteration with drugs**







# Contamination

with undeclared drug ingredients

- **Corticosteroids** –

- strong enough to cause Cushing's disease

- **Anabolic steroids**

- **Toxic levels of cadmium, lead, arsenic**

- **Prescription antibiotics**

- **Sedatives**

- **Narcotics**

- **Viagra**

- **Sibutramine** ( appetite suppressant)





# Alteration of Drug Clearance due to “herbs”

## Detoxification system - liver

### Cytochrome P450 & CYP3A4

#### Examples -

- Cat's claw
- Chamomile
- Garlic
- Echinacea
- Licorice
- Marijuana
- St. John's wort
- Water cress





# St. John's wort/ Drug Interactions

**> 57% reduction in Indinavir concentrations**

- Cy P450 interaction
- St. John's wort/cyclosporine-heart transplant rejection
- *Lancet Feb 12, 2000*





# Anesthesia & “Herbs”

The American Society of Anesthesiologists recommends the discontinuation of these herbs at least **two weeks** prior to surgery.



- **Ginger, ginseng, feverfew, ginkgo, and garlic** may alter coagulation.
- **Licorice** may cause hypokalemia
- **Valerian, Kava & St. John's wort** may interact with anesthetic barbiturates, hypnotics & benzodiazepines.
- **Ephedra** – cardiovascular effects of anesthetic agents.
- **Herbs and Anesthesia**, [Alternative Therapies in Women's Health](#) | April 2001 Carol L. Norred, CRNA, MHS,





# Major Categories of “Herb” Effects

- Antioxidant
- Anti-cancer
- Anticoagulant
- Arthritis relief
- Hormone-related
- Immune Modulating
- Lipid Lowering
- Mood/Mind altering
- Weight Loss





# Antioxidants

- **Vit A, Vit C, Vit E, alpha lipoic acid, pycogenol, ginkgo, grapeseed extract, selenium...**
- **Excess protect cancer cells ?**
- **Excess produces Pro-oxidants?**
- **Alters excretion of drugs?**





# Antioxidant Botanicals

- **Alpha lipoic acid**
- **Pycogenol (Marine pine)**
- **Grapeseed extract**
- **Ginkgo**
- **Hawthorn**
- **Ginseng**
- **Green tea**
- **CoEnzyme Q10**



# Antioxidant –Co Enzyme Q10

Given routinely in Japan, Russia and Europe for Heart Disease

Possibly Effective for: *(from fermented beets, not animal derived)*

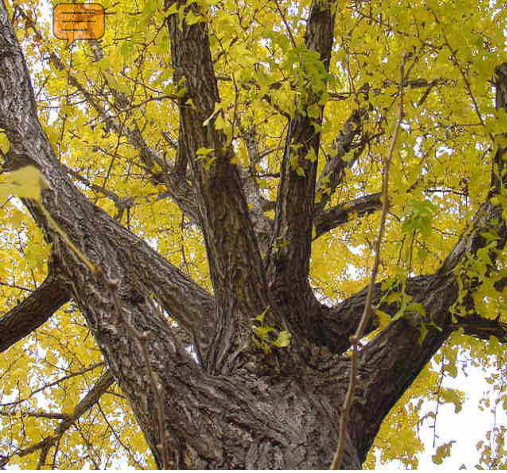
- Congestive heart Failure
- Reducing risk of 2<sup>nd</sup> heart attack
- Reducing hypoxic damage ( after heart bypass)
- Repleting Co EnzQ10 levels lowered by statin drugs
- Reducing cardiac toxicity from ARA-C chemo
- Improving blood pressure
- Neurological conditions
  - Huntington's Dz, Muscular Dystrophy....
  - Slow decline in Parkinson's Dz
- Reducing frequency of Migraines ( 30%)
- Improving immunity for those with HIV

## Moderate interaction w/ anticoagulants

- No reports of significant adverse events
- Could antagonize warfarin







# Antioxidant – Ginkgo biloba ( 2 lobes-leaves)

## Possibly Effective for:

- “Improved thinking” - young and old
  - Short term visual memory
  - Speed of mental processing
- Inconsistent data with dementia
- Improved color vision-DM retinopathy
- *Antioxidants from leaves* –
  - involved in blood vessel repair
  - seem to improve circulation- brain
- Associated with decreased risk of overall mortality
- Blood thinner
  - not to be taken with aspirin, garlic, ginger, Coumadin





# Antioxidant - Green Tea

## EGCG, Epigallocatechin Gallate

**Contains antioxidant polyphenols**



**Possibly Effective for...**

- Reducing the risk of several types of cancer
- Reducing risk of Parkinson's disease.
- Hyperlipidemia



**Antiplatelet activity**

- **Can prolong bleeding time**

Liver toxicity with high dose polyphenol supplements?



# Anticoagulants

- Clove
- Garlic
- Ginger
- Ginseng (Panax)
- Red Pepper
- Willow (aspirin)
- Red Clover (coumarin)
- Shitake mushroom





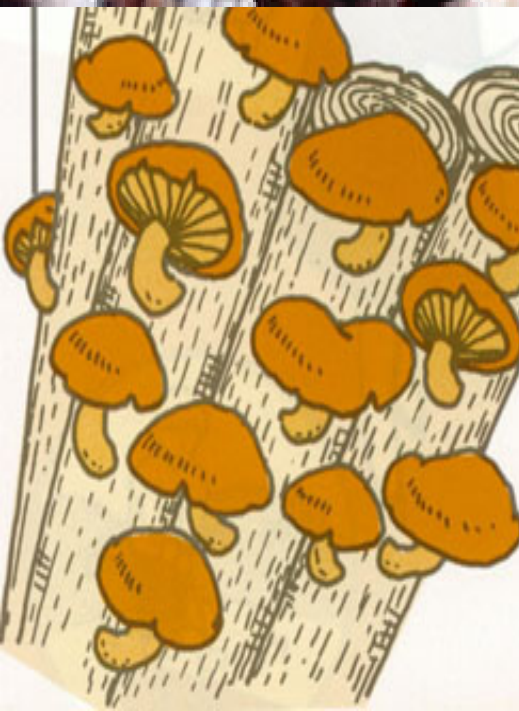
# Ginger

- **Anticoagulant** at >500 mg.
- **Antiemetic** 2-4 grams  
as effective as Reglan at  
preventing nausea/vomiting  
associated with chemotherapy
- Seasickness -as effective as  
Scopolamine
- May raise blood pressure
- Anti-inflammatory benefits



# Shitake Mushrooms

- Human Studies (oral or IV)  
**anti-tumor effects**
- Appears to stimulate macrophages, killer cells and T- lymphocyte production
  - **Inhibition of platelet aggregation**
  - **Hypotension**





# Immune Modulating

- Astragalus
- Cat's Claw
- Echinacea
- Green Tea
- Shitake/Reishi





© Steven Foster

# **Astragalus      Huang Ch'i**

## Numerous Immune Effects

- Stimulates Interferon
- Enhances macrophage activity
- Antiviral
- In vitro T- cells of cancer pts + 260%
- Used along with chemotherapy & radiation in China -
- Less side effects,
- Improved survival time



# Cat's Claw

## Una de Gato

- Vine - South America
- Immune stimulant history
- Clinical benefit in acute leukemia.
- NCI Natural Product Branch found insufficient antineoplastic activity
- [ Didn't look at possible immune benefits]
- Inhibits platelet aggregation.





## Immunity Effects- Echinacea

- Reduced severity and length of cold
- Should not be taken chronically- or by those with Diabetes, MS, HIV, TB, collagen diseases.
- Best if used as needed (onset of cold) <3 days.
- **Preliminary evidence of enhanced longevity for patients with advanced cancer**



# Natural medicines for Cancer treatment?

**Potential for benefit in controlled  
studies:**

**Astragalus**

**Cat's Claw**

**Echinacea**

**Herbs touted for cancer but too toxic:**

**Pau D'Arco**

**Chaparral**

**Mistletoe**

***Toxic: Graviola***

**No Evidence of Benefit:**

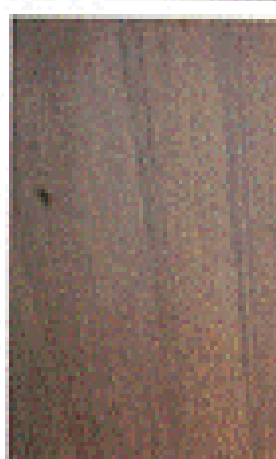
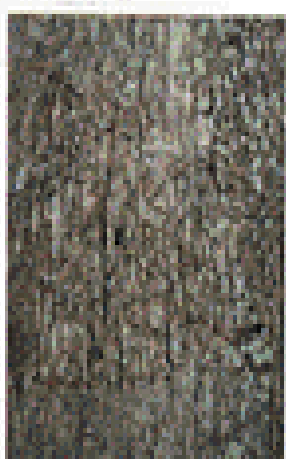
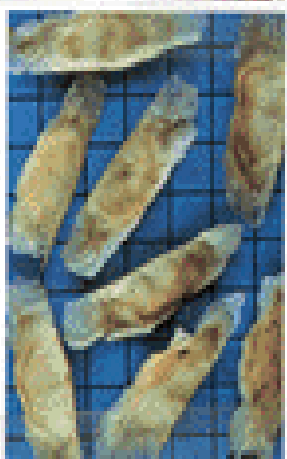
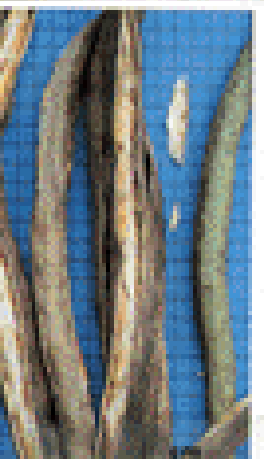
**Essiac, Shark Cartilage, Seaweed**





# Pau d'Arco Lapecho

- Anti-tumor agent
- Too toxic
- Significant plasma levels couldn't be obtained without **severe side effects**
- Leads to weight loss, anticoagulation





# Chapparal

- American Indian Cancer “Remedy”
- Liver toxic

Woman self-medicated  
x 5 months

- **required a liver transplant**



# Mistletoe Iscador

- **10/11 Clinical Studies Showed Improved Survival.**



- The 1 negative study had the best methodology though
- Used as anticancer agent in Europe since the 1960's.
  - Numerous poisonings
  - **Pts should never self-medicate with this**



# Dietary Supplement Concerns

*Sites look legitimate:  
-but sell toxic substances*

*“Graviola- Cancer Cure”*



**NATURAL MEDICINES**  
COMPREHENSIVE DATABASE



*(Reliable, scientific resource  
Provides pt information sheets):*

## **GRAVIOLA**

- **How does it work?**
- Graviola contains many chemicals that may have antimicrobial and anticancer effects.
- **Are there safety concerns?**
- **Graviola can kill nerve cells in the brain and other parts of the body.**
- **It should NOT be used.**

**Do not use graviola if:**

**You have Parkinson's Disease or another condition involving nerve function.**



## **False Anti-Cancer Claim- Essiac**

from RN Rene “Caisse” backwards -  
“Indian cancer remedy”

FDA: Detention & surveillance for

**False Claims**



NCI & Canadian Fed Health Dept:

**No Benefit**

77 case reports:  
47 no benefit, 17 died,  
5 required fewer analgesics,  
8 had objective response or were stable.





# False Anti-Cancer Claim – Shark Cartilage

“Sharks don’t get cancer”

- *They do - and in their cartilage*

**No benefit proven when taken by  
mouth**

**Can cost >\$900/month**

**NCI study 1998 disproved benefit  
for cancer**







## Liver Effects- Milk Thistle

- **Protects liver** cells from damage of mushroom poisons and alcohol
- Human trials: **beneficial for cirrhosis** and hepatitis of various origins
- **Infusion prior to certain chemotherapy** reduced kidney toxicity without interfering with antitumor effect.



# Fish Oil

In animal studies

- Reduced cancer growth
- Reduced metastasis

Effective for:

Reducing Triglycerides 20-50%

Likely Effective for:

- Slowing weight loss in end stage cancer
- Reducing death from heart disease
- Preventing heart disease and heart attack
- Reducing renal damage with CSA

Flax seed oil not shown to be effective

Increased risk of bleeding if >3 grams per day

Caution pts not to use Cod liver oil ( too high in Vit A)





# Natural Substances Used to Offset Menopausal Symptoms:

- Black Cohosh
- Don Quai / Angelica  
[contains a carcinogen]
- Vitex /Chaste Tree
- Phytoestrogens
  - **Soy foods, flax, sesame or isoflavone supplements**





# Black Cohosh

- ***Conflicting Data***
- Randomized controlled DB trial
  - **breast cancer survivors-**symptoms improved in both placebo and Black Cohosh group
- ***Possibly Effective for reducing menopause-related: hot flashes, excessive sweating, irritability, poor sleep, palpitations, headaches***
- **Effects of long-term use not known.**
  - Should not be used >6 mos. at a time.
- **Taken by millions**
  - 1 case of liver failure
  - a few reports of liver damage (with other drugs and alcohol being used)



# USP –Black Cohosh caution

- **The U.S. Pharmacopeia**

*(the standards-setting organization for foods and drugs)*

advises that **Black Cohosh** products be labeled with the following cautionary statement:

- **"Discontinue use and consult a healthcare practitioner if you have a liver disorder or develop symptoms of liver trouble, such as abdominal pain, dark urine, or jaundice"**
- **Menopause 15:628-638, 2008.**





# Phytoestrogens?

Those from soy, sunflower seeds, flax, sesame seeds decrease potent estrogens

- **Associated with lower rates of cancer**
- **Inhibit breast cancer and prostate cancer growth in animal studies**
- **may slow the growth of prostate cancer in men**
- **3 cups soy milk, 1 c tofu, 1/2 c roasted soy nuts/day**
- **In Postmenopausal Women- apparent estrogen effects without increasing Estrone or Estradiol [ no effect on breast]**



# Dietary Supplement Ingredients Touted for Weight Loss

- **Stimulants** – **Gurana, Mate, Caffeine, Theophylline, Theobromine, Ephedra**
- **Diuretics**
  - **Horsetail**
  - **Uva ursi**
  - **Nettle**
- **Fibers**      **Chitin, guar gum, pectin...**
- **Licorice** - flavoring in wt loss teas  
[pseudoaldosteronism, CHF, low K, MI]
- **Hoodia Gordonii** **Trimspa**  
**African cactus “substance p57”**



# KRIMSPA

Be Envied.

# Anna Nicole Smith



**Naringine** →  
 is the compound in grapefruit that interacts with so many drugs (like Cyclosporine)

## BEFORE

## AFTER

### Supplement Facts

Serving Size: 2 Tablets

Servings per Container: 30

	Amount Per Serving	% DV
Chromium (as chromium dinicotinate glycinate)	150 mcg	125
Vanadium (as vanadium amino acid chelate)	30 mcg	*
Glucomannan†	400 mg	*
Sodium carboxymethylcellulose	100 mg	*
Citrus naringinine	10 mg	*
Glucosamine HCl††	100 mg	*
Cocoa extract (standardized for PEA (Phenylethylamine, tyramine and 10% theobromine))	325 mg	*
Green Tea extract (40%) (standardized for (ECGC) epigallocatechin gallate, polyphenols and 40% caffeine)	250 mg	*
Hoodia gordonii cactus (whole plant/less roots)	150 mg	*

\*Daily Value (DV) not established.

Other ingredients: dicalcium phosphate, microcrystalline cellulose, croscarmellose sodium, stearic acid, magnesium stearate.





# Ginseng

**\$500-\$3,000 per pound**

- May lower glucose
- Immune stimulation
- Could alter blood pressure
- Can reduce clotting time
- **American Ginseng** – **Possibly Effective** for:
  - Reducing postprandial glucose – DM type2
  - Reducing respiratory infections
- **Panax Ginseng** – **Possibly Effective** for:
  - » Improving abstract thinking
  - » Erectile dysfunction
    - Possibly unsafe if used long term ( > 3 mos.) d/t hormone effects
- **Siberian Ginseng** – **Possibly Effective** for:
  - Reducing frequency, severity & duration of Herpes simplex 2 (HSV2)



# Placebo Effect

- is most effective when measured outcomes are:

**Changes in behavior/attitude**

**Subjective sensation (pain/discomfort)**

**Responses controlled by endocrine glands or ANS:**

- **blood pressure**
- **acid stomach**
- **asthmatic breathing:**

= the same conditions commonly treated with herbs





# Male Products- Saw Palmetto

- **Anti-inflammatory, diuretic**  
- improves urinary flow in Benign Prostate Hypertrophy
- As effective as Finasteride  
- less S/E, quicker onset of benefits [JAMA Nov 98]
- **May alter PSA /hormones**





# PC-SPES to slow Prostate cancer?



Saw palmetto, skullcap, chrysanthemum, licorice, ginseng, reishi mushroom [9 herbs]



- Estrogenic effects
- Used by >8,000 men



# PC-SPEs

- Feb. 8, 2002 withdrawn from the market
- Contaminated with:  
Coumadin, Indomethacin  
and DES
- USDA warnings





## Hormone Products- **DHEA**

- Testosterone and estrogen precursor
- May stimulate the growth of hormone-sensitive cancers:
  - **Breast, ovarian, testicular, prostate**
  - **Untested in long-term trials**
  - **Many side effects**





# Mind Effects- Melatonin



- Hastens sleep and may reduce jet lag
- Anticancer (nurses' study – night shift workers- less melatonin/ higher risk of cancer)
- Normal production in your body  
.03 milligrams a day
- May induce depression
- Amounts sold >50 mg !
- It would take you 5 years to make that much !





## Mind Effects- St. John's Wort

- Shouldn't be taken with Selective serotonin reuptake inhibitors [i.e. Prozac]
- Decreases contraceptive drug levels by > 13%
- Photosensitizer
- Commission E :
  - **More effective than placebo for mild to moderate depression**
  - **Less S/E than standard antidepressants**
- Banned in France.
- Japan, the United Kingdom, and Canada are in the process of including drug-herb cautionary language on St. John's wort products







## Sleep Aids/ Anti-anxiety

- Kava

**Double-blind clinical studies indicate effective for mild-moderate anxiety, less side effects than standard medications**

- **Initial Concerns:**

**“Driving under the influence”**

**Skin disorder, liver & kidney abnormalities**

**Concern for Interactions with similar drugs**

- **Recent concerns:**

**68 cases of liver toxicity.**

**Banned –Switzerland, Germany & Canada**



# Sleep Aids/ Anti-anxiety

■ Valerian

■ Passionflower

- appear safe & effective

- i.e. “Nighty Night” tea

*Traditional Medicinals*

■ Concern for augmenting effects form similar drugs





# **Vitamins/Minerals?**

## **Often Inadequate in American Adults' Diets:**

**Magnesium, B6, Folic acid  
and Zinc**

## **Rarely Optimal in Diet:**

**Vitamin E, C, A**

**Frequently Deficient**

**Vitamin D ( not due to diet):**





# Micronutrient Deficits/ Immune Effects

## ■ Low Vitamin A

↓ Thymic wt

↑ bacteria binding-respiratory epithelium

↑ death from respiratory infections ( i.e. measles)

## ■ Low B<sub>6</sub>

↓ B & T lymphocyte proliferation

↓ IL2 production

## ■ Low Vit C ↓ bactericidal activity





# Foods Vs. Supplements

## **Superior absorption from food**

- i.e. milk protein (casein), lactose & Vit D improve Calcium absorption from milk



## **Supplements Compete for** absorption –

- i.e. Zinc, Calcium & Iron supplements



## **Potential Toxicity from supplements**

no toxicity from high intake of the same nutrients from food

(i.e. calcium, folic acid, Vit E, B-carotene)

# Vitamin D- Differentiating Agent

- Low Vitamin D is associated with increased rates of all types of cancer
- Over 200 genes have receptors for Vit D
- Tumor suppressor protein p53 and growth factors are regulated by Vit D
- **African American men with prostate cancer –**
  - Same incidence of prostate cancer as white men
  - Death rate 7 x that of white American men
    - thought due to Vit D deficiency





# Vit D reduces cancer risk

## Risk for deficiency:

- Location far from equator  
>35 degrees latitude
- Dark skin
- Obesity
- Age>50



i.e. Bethesda , Maryland (37 degrees latitude)

November through March, inadequate UVB rays;





# Vit D — “the numbers”

- **To Test Your Vit D status: 25-OH Vit D**  
( not 1,25 Vit D).
- **Goal reference range > 32 ng/mL** or > 80 nmol/L  
[>20 ng/mL per IOM Nov 30,2010]
- **Sun on skin can create 10,000 IU** (<20 mins.)  
before your skin turns pink
- **To treat deficiency ~ 50,000 IU Vit D**  
once a week for 6 months until levels are normal - then 2,000 IU/day
- **If You are at risk for Deficiency?**  
**800 to 20000 IU/day** —most Vit D experts
  - The 11/30/10 RDA: 600 IU/day for adults<70 yrs;  
800 IU/day for those over 70
  - The new upper intake level [UL] : 4,000 IU/day.
  - Vit D researchers argue that 10,000 IU/day should be the daily max

Heaney, RP The Vitamin D requirement in health and disease. Journal of Steroid Biochemistry and Molecular Biology. 2005; 97:13-19.



# Diet Effects- Protein- Amino Acids **Glutamine -**

**Primary fuel**

**– for rapidly proliferating cells**

- **during injury, sepsis, presence of tumors**



**↑ tumor cell kill -XRT & Chemo**

**↑ natural killer cell activity**

**↓ mortality and morbidity from chemotherapy.**





# Glutamine

- Auto BMT: reduced mucositis  
n=193 BMT patients

**1 g/m<sup>2</sup> 4x/day as “swish/swallow”**

**Less mouth pain (opiate use) p<0.005**

**Allo BMT no change in mouth pain  
but increased 28 day survival**

- Reduced veno-occlusive disease -  
preserved liver function n=34 BMT pts.
- reduced incidents of sepsis for pts. on  
cyclosporine





# Botanical Medicine RESOURCES

- **The Natural Medicines Comprehensive database**

<http://www.naturaldatabase.com/>



**NCCAM** National Center for  
Complementary and Alternative Medicine

<http://nccam.nih.gov>



<http://dietary-supplements.info.nih.gov/>

