



## GRAND ROUNDS CALL SUMMARY

April 12, 2017

Every 2nd Wednesday

5:30 PM Pacific / 6:30 PM Mountain / 7:30 PM Central / 8:30 PM Eastern

**Clinical Pearl:** NLR: Neutrophil to Lymphocyte Ratio as a prognostic and predictive biomarker

**Therapeutic Goal:** Most studies less than 4, per Dr. Dwight McKee: less than 2

Given the ease of its calculation from routinely measured blood tests without additional costs, the NLR could result in clinical translational advances in the identification of high-risk cancer patients, which could aid in clinical decision making.

**REVIEW: One hundred studies comprising 40,559 patients** were included in the analysis, 57 of them published in 2012 or later. **Median cutoff for NLR was 4.**

**Overall, NLR greater than the cutoff was associated with a hazard ratio for OS of 1.81 (95% CI = 1.67 to 1.97; P < .001), an effect observed in all disease subgroups, sites, and stages.**

**Neutrophils and other cells such as macrophages have been reported to secrete tumor growth-promoting factors, including:** VEGF vascular endothelial growth factor, hepatocyte growth factors, IL-6, IL-8, MMP matrix metalloproteinases and elastases and **thus likely contribute to a stimulating tumor microenvironment.**

(*JNCI J Natl Cancer Inst (2014) 106(6): dju124 doi:10.1093/jnci/dju124*)

### Prognostic and predictive biomarker in multiple cancers

- Associated with advanced pathologic tumor stage
- Increased cancer-specific mortality
- In solid tumors can predict OS, PFS and distant metastases recurrence, survival
- NLR was significantly and negatively associated with overall survival in advanced cancer patients.
- Large number of studies in multiple cancers including lung breast, prostate colorectal, ovarian urologic: bladder, ureter and kidney, oral squamous cell, esophageal, cervical, testicular, neuroendocrine, biliary

**Useful in assessing response to immunotherapy treatments (measure prior and during tx)**

### Interventions: Shifting the ratio

- Beta Glucans shifts protumorigenic neutrophils to tumor suppressing neutrophils
- Plant polysaccharides have been shown to possess antioxidant, anti-inflammation, cell viability promotion, immune-regulation and antitumor functions in a number of disease models

### **>> Astragalus root (polysaccharide-Astragaloside IV) 2-4 grams per day**

- Suppresses NFkB activation and inflammatory gene expression
- Suppresses proinflammatory factors TNFa, IL1B1, IL6
- Inhibits neutrophils adhesion and infiltration

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[Am J Chin Med. 2016;44\(3\):463-88. doi: 10.1142/S0192415X16500269. Epub 2016 Apr 24.](#)

*The Anti-Oxidant and Antitumor Properties of Plant Polysaccharides.* [Jiao R1](#), [Liu Y2](#), [Gao H3](#), [Xiao J4,2,5](#), [So KF5,6,7](#).

[Am J Chin Med. 2016;44\(1\):1-22. doi: 10.1142/S0192415X16500014. Astragalus membranaceus: A Review of its Protection Against Inflammation and Gastrointestinal Cancers.](#) [Auyeung KK1](#), [Han QB2](#), [Ko JK1](#).

[The Anti-Oxidant and Antitumor Properties of Plant Polysaccharides.](#) [Jiao R](#), [Liu Y](#), [Gao H](#), [Xiao J](#), [So KF](#).  
*Am J Chin Med. 2016;44(3):463-88. doi: 10.1142/S0192415X16500269.*

## >> Curcumin (Rhizoma Curcuma Longa) 2-6 grams per day

- Inhibits COX 2, NFkB, TNF $\alpha$ , IL6, IL1, CRP, LOX 5

### Drug Interactions

Anticoagulant agents (-inhibits platelet aggregation), aspirin, clopidogrel (Plavix), diclofenac (Voltaren, Cataflam, others), ibuprofen (Advil, Motrin, others), naproxen (Anaprox, Naprosyn, others), dalteparin (Fragmin), enoxaparin (Lovenox), heparin, warfarin (Coumadin)

Chemotherapy agents: Ifosamide, Methotrexate

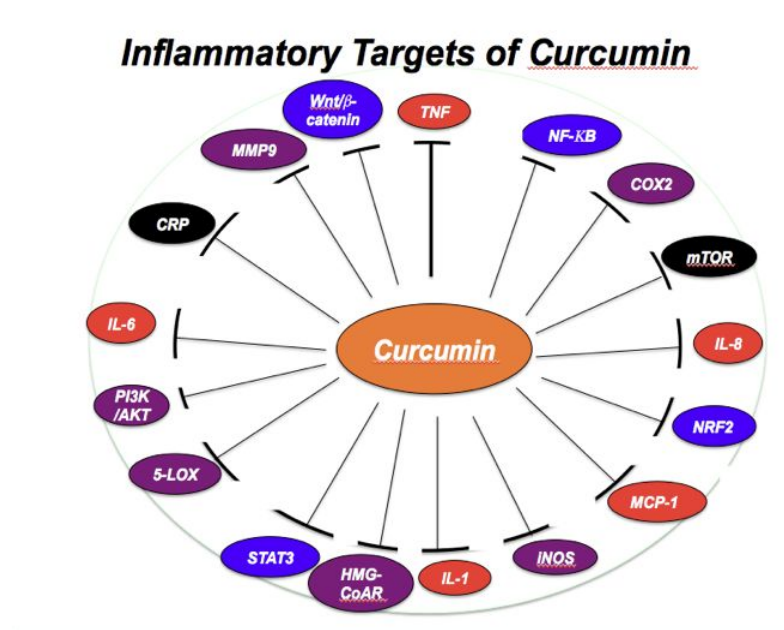
Caution: thrombocytopenia

*Exp Ther Med.* 2015 Nov; 10(5): 1615–1623. Published online 2015 Sep 17. doi: [10.3892/etm.2015.2749](https://doi.org/10.3892/etm.2015.2749)

PMCID: PMC4665301 Biological and therapeutic activities, and anticancer properties of curcumin

Donatella Perrone, et al

*Altern Med Rev.* 2009 Jun;14(2):141-53. Anti-inflammatory properties of curcumin, a major constituent of Curcuma longa: a review of preclinical and clinical research. [Jurenka JS](#)



### NLR Selected References

Mantovani, A., Allavena, P., Sica, A. & Balkwill, F. Cancer-related inflammation. *Nature* 454, 436–444 (2008).

Ahn, H. K. et al. Neutrophil-Lymphocyte Ratio Predicts Survival in Terminal Cancer Patients. *J Palliat Med.* 19, 437–441 (2016).

Nakamura, Y. et al. Neutrophil/lymphocyte ratio has a prognostic value for patients with terminal cancer. *World J Surg Oncol.* 14, 148 (2016).

Wang, F. et al. Changes in neutrophil/lymphocyte and platelet/lymphocyte ratios after chemotherapy correlate with chemotherapy response and prediction of prognosis in patients with unresectable gastric cancer. *Oncol Lett.* 10, 3411–3418 (2015).

Guthrie, G. J. et al. The systemic inflammation-based neutrophil-lymphocyte ratio: experience in patients with cancer. *Crit Rev Oncol Hematol.* 88, 218–230 (2013).

## Case Study Submissions:

Case Study	<b>Patient “PM”</b> - Submitted by Judy Pruzinsky, L.Ac.
Brief Summary	<p>62 yo male - 2/3/17 Colonoscopy Dx - 3cm sigmoid cancerous tumor, stage unknown            CAT scan - no metastasis in the torso            PET scan - to be arranged soon            Labs:</p> <ul style="list-style-type: none"> <li>● Low Vit D 24</li> <li>● High Cholesterol, total 231</li> <li>● HEAVY METALS ARE BLOOD LEVELS</li> <li>● High Cadmium</li> <li>● High Cesium</li> <li>● V. High Lead</li> <li>● V. High Mercury</li> </ul> <p>Hx of hypertension and high blood pressure (150/90)            Family Hx - Sister died at age 37 metastasized breast cancer, Sister with breast lumpectomies at age 58</p> <p>Oncology recommending surgery (removal of 15 inches) right away.  <b>Patient wishes to delay surgery to try other treatments/options.</b></p> <p>Current Diet:</p> <ul style="list-style-type: none"> <li>● Alkaline foods</li> <li>● No raw fruits or vegetables</li> <li>● No sugars except what is in coconut water.</li> <li>● Added sauerkraut and other fermentations, goat bone broth</li> <li>● ghee as only dairy</li> </ul> <p>Current Supplements:</p> <ul style="list-style-type: none"> <li>● green tea, antioxidants, curcumin with piperine—c. 1900 mg.</li> <li>● multi-vitamins, potassium—200 mg.</li> <li>● Probiophage—15 billion</li> <li>● vitamin D—10,000 mg.</li> <li>● salmon oil—4000 mg.</li> </ul>
Recommendations	<p>Considerations:</p> <ul style="list-style-type: none"> <li>● Risk of GI Obstruction? Treatable cancer? Likelihood of progression?</li> <li>● Most likely surgical resection will give patient the most protection (only 62 yo) from recurrence, progression and metastasis over lifetime. If he wishes to do AGGRESSIVE integrative approach, then he can exert control over tumor and tumor microenvironment.</li> <li>● Protein repletion is important: 60 grams per day - for immunity and for preservation of muscle mass.</li> <li>● Changing diet, Tai Chi and nutritional supplements alone will not eradicate cancer. Must have a more comprehensive plan, include all factors in tumor microenvironment and a plan to support tumor control. He can certainly consult with a ND and explore IVC, IV Artesunate, IV Curcumin, IV Mistletoe</li> <li>● Adjuvant chemotherapy is often a starting place to reduce the size of the tumor so that a smaller surgery can be performed, and so a second oncology opinion may be warranted</li> </ul>

## Questions & Answers

### 1. Denny Thompson, DC:

*I noticed that the you do not use PaleoCleanse in your recommendations. Is there a reason?*

- a. PaleoCleanse is a product through Designs for Health
- b. It is important to supporting detoxification pathways in all patients
- c. Consideration for using products where this is a high level of compliance, some patients struggle with PaleoCleanse due to the sulfur taste
- d. Awareness of drug nutrient and drug herb interactions

- e. Ongoing support for detoxification vs doing a CLEANSE
- f. Precision medicine:
  - i. Consider genomics
  - ii. Consider all doorways of detox and elimination (Liver, Kidney, Intestines, Skin)
  - iii. Consider age, personal health history, frail vs robust, weight, digestive capacity, microbiome, sensitivities, level of motivation and capacity to engage fully, compliance, lifestyle factors

## 2. Shiroko Sokitch, MD/Acupuncturist:

*A patient of mine has a recurrent breast cancer with mets to her spine and hip bones. She had radiation and is on oral chemo and very tired. Because of budget constraints she doesn't see me much and isn't open to doing labs that would cost her money. She craves sugar and I am not sure that she isn't still eating it. Any thing I can give her that will help?*

### Considerations with info provided

Which TYPE of breast cancer?

Age? Pre or Post MPX? Bone Density?

Digestive capacity - ability to absorb nutrients?

Current lifestyle - sedentary-active?

Stressors?

Good support system?

Emotions, Motivation, Coping, Resilience?

What are her attitudes about life, death, survival?

What is she willing to do?

What is her body type? Weight, body composition?? (ADIPOSE TISSUE: adipokines, inflammation, estrogens, leptin)

### Goals - Patient Teaching - Intervention

**Take control of tumor microenvironment** (signaling, gene expression, immune modulation)

No \$\$\$ - What can be accomplished with diet and lifestyle, emotions, spirit, resilience?

Diet: nutrient density, protein repletion, fermented foods, eat the rainbow-plant pigments and phytochemicals, healthy fats and oils (chia and hemp seeds, walnuts, olive oil, avocados, omega 3 eggs), soy isoflavones (non GMO traditional soy foods)

Drink green tea - 2-4 cups daily

Superfoods: avocado, asparagus, Shitake Mushrooms, berries, fermented foods, almonds, almond butter,

Her plate: HALF COLORFUL VEGETABLES, Quarter: clean protein, 1/8th healthy fats and oils

Low glycemic, no alcohol

Lifestyle - exercise, sleep, relaxation, stress management

Yoga, Tai Chi, Time in Nature, Weight Bearing exercise, Meditation, Visualization, Community

A few supplements

Curcumin 2000mg/day (fat soluble)

Vitamin D 5000 iu + Vit K (K2 most important)

Vitamin D3 5000 IU (as Cholecalciferol)

Vitamin K 550 mcg (as Vitamin K1 Phytonadione 500 mcg; Vitamin K2 Menaquinone-7 50 mcg)

Probiotic or eat fermented food and insoluble fiber daily (healthy microbiome)

Bone Minerals (copper free formula) with Genestein

### PRECISION MEDICINE and Individualization--Assess Tumor Microenvironment

Use a discount online lab like Direct Labs (QUEST at 1/3-1/2 off retail)

Order CMP, CBC +Diff, Cu, Cp, Zn, Fibrinogen activity, D-Dimer, hs CRP, Bone ALK Phos, Ionized Ca++, Fasting

Insulin every 3-6 months (perhaps she can crowdfund from family and friends..probably \$200-\$300)