Inflammation

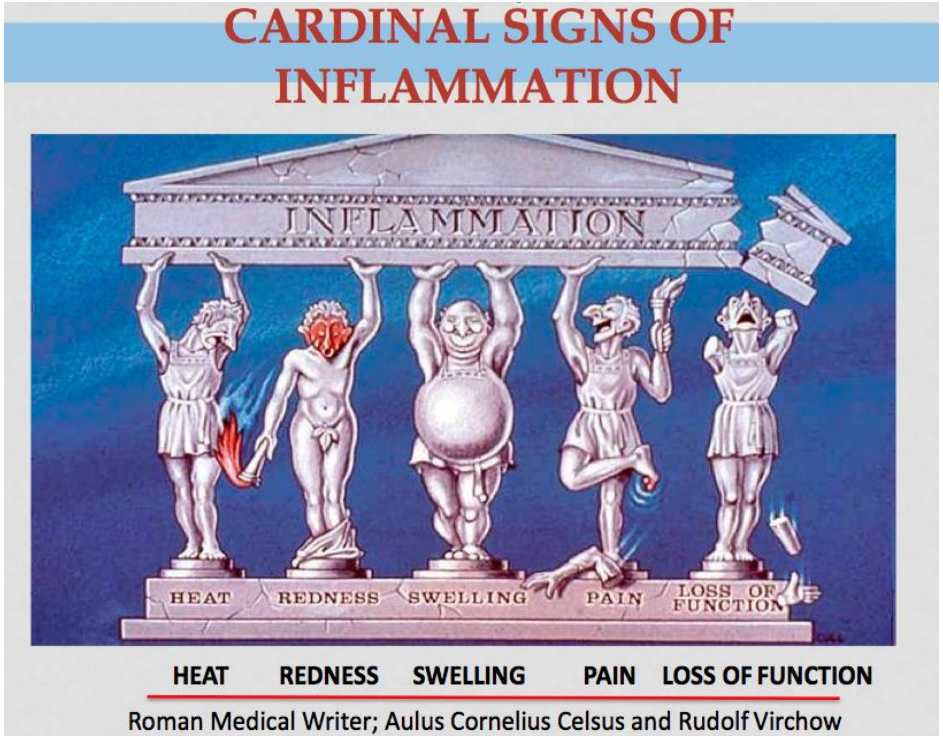
Yoga for Chronic Pain

What is inflammation?

“A reaction of the host to infectious or sterile tissue damage and has the physiological purpose of restoring tissue homeostasis”

From Latin ‘inflammatio’ = ‘to set fire to’

- Defined by four cardinal signs
- Calor, rubor, tumor, dolor
- heat, redness, swelling, pain
- Functio laesa (loss of function)



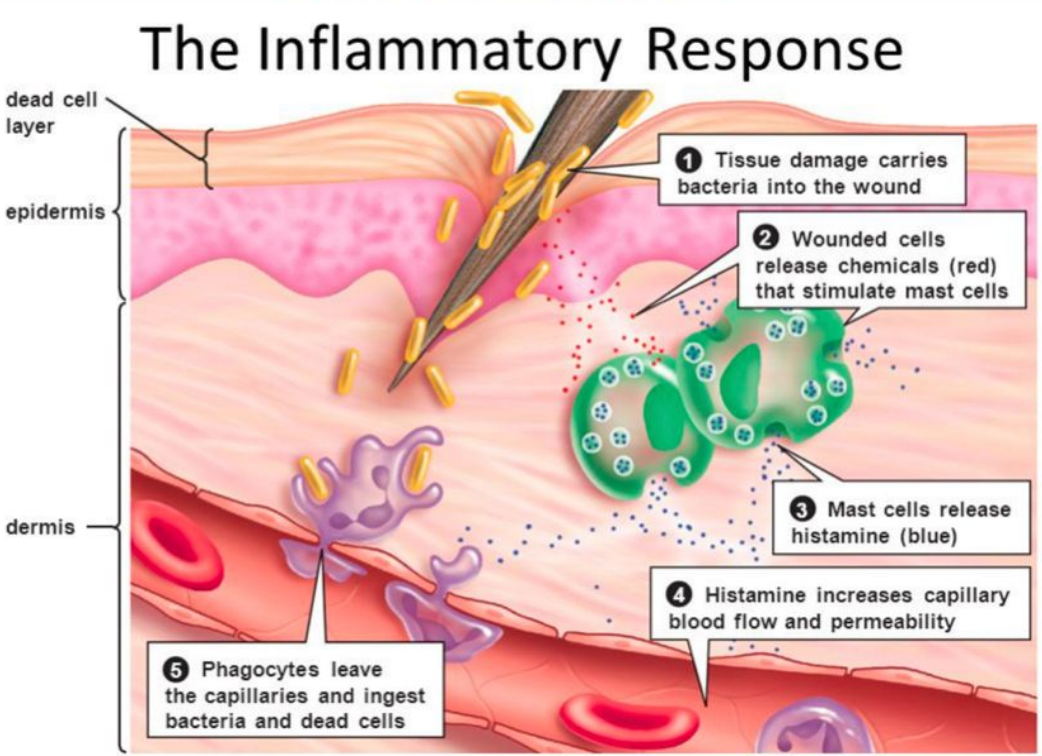
Acute versus chronic inflammation

Paradoxically, inflammation is both absolutely essential for staying alive AND the leading cause of disease/death!

- The body's fundamental protective response to injury (**acute/physiological**) AND
- The driving force behind aging and most major human diseases (**chronic/ pathological**)

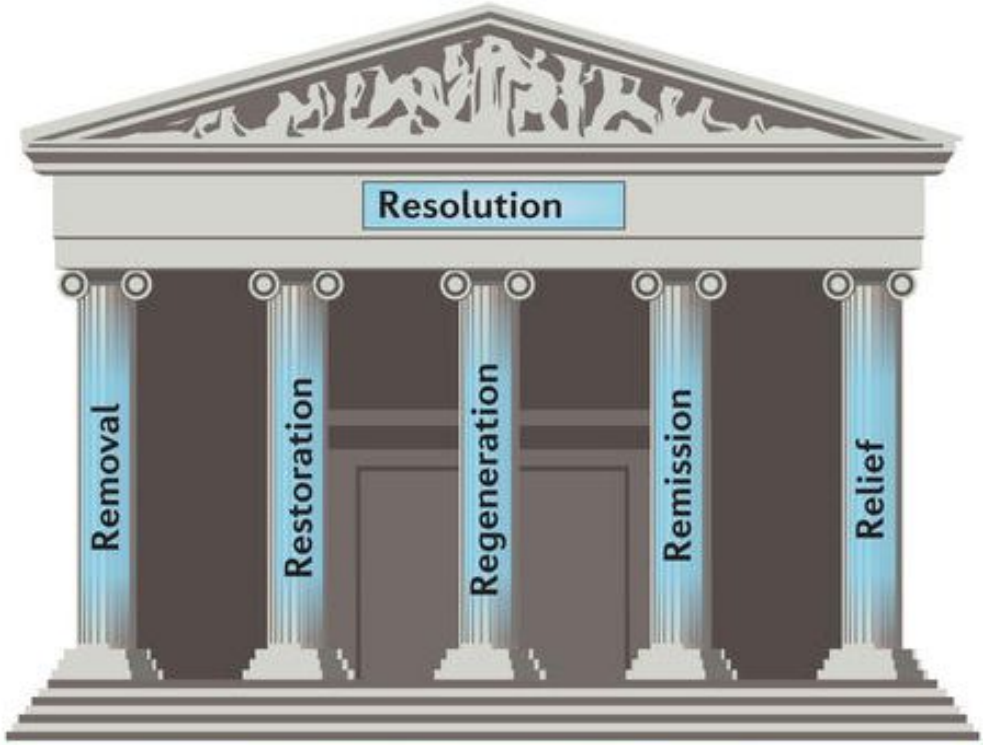
	Acute inflammation	**Chronic inflammation**
Duration:	days	weeks to years
Onset:	immediate/rapid/obvious	delayed/gradual/insidious
Cardinal signs: (heat, redness, swelling, pain, loss of function)	present/obvious (all have physiological function)	may be absent/hidden
Type of response:	physiological	pathological
Consequences for body:	positive = healing injury/ fighting infection & staying alive	negative = disease & death
Involved in:	injury (sterile tissue damage), infection (stubbed toe, sprained ankle, splinter)	● classical inflammatory diseases - rheumatoid arthritis, ulcerative colitis, hepatitis, bursitis, dermatitis ● many conditions not previously thought to have inflammatory component such as atherosclerosis, cardiovascular disease, cancer, Alzheimer's, depression, obesity & type 2, diabetes = 'diabesity'
	short-term, self-resolving process ● injured area sends out signals (histamine, cytokines) ● immune system comes in and eliminates invaders ● eventually activates repair of tissue damage	caused by: ● ongoing pro-inflammatory processes such as persistent insult (foreign body or infection) or disease process (autoimmunity) ● failure of normal mechanisms that resolve acute inflammation

INITIATION OF ACUTE INFLAMMATION



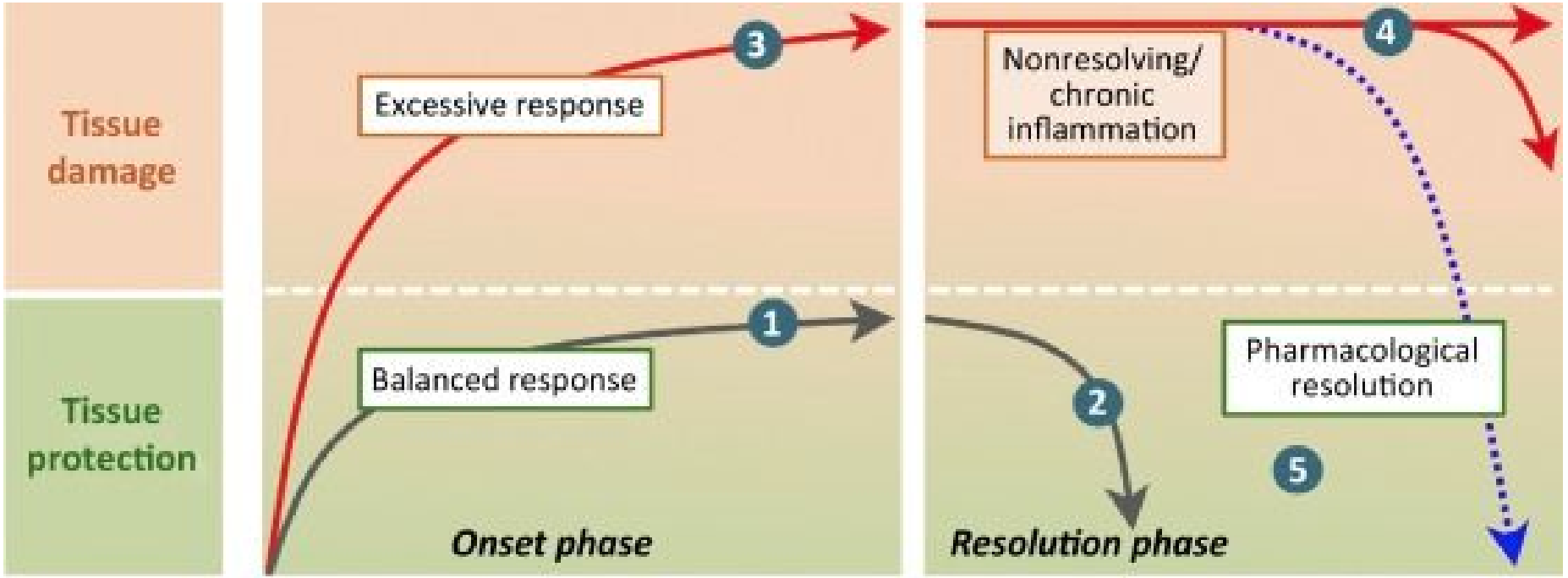
Chronic inflammation = failure of resolution

- Resolution of acute inflammation is active process
  - crucial to avoid persistent chronic inflammation
  - also drives activation of tissue repair mechanisms
    - necessary for return of local tissues to homeostasis
  - requires production of molecules called ‘resolvins’
    - resolution phase mediators (RPMs)
    - act as 'stop-signs' to the inflammatory process.
    - initiate the rapid resolution of inflammation so that tissue healing can begin
    - produced from from omega-3 fatty acids (EPA & DHA from fish, krill or algae)
    - aspirin enhances conversion of omega-3 into resolvins
- If acute inflammation fails to resolve properly
  - progresses to persistent chronic inflammation



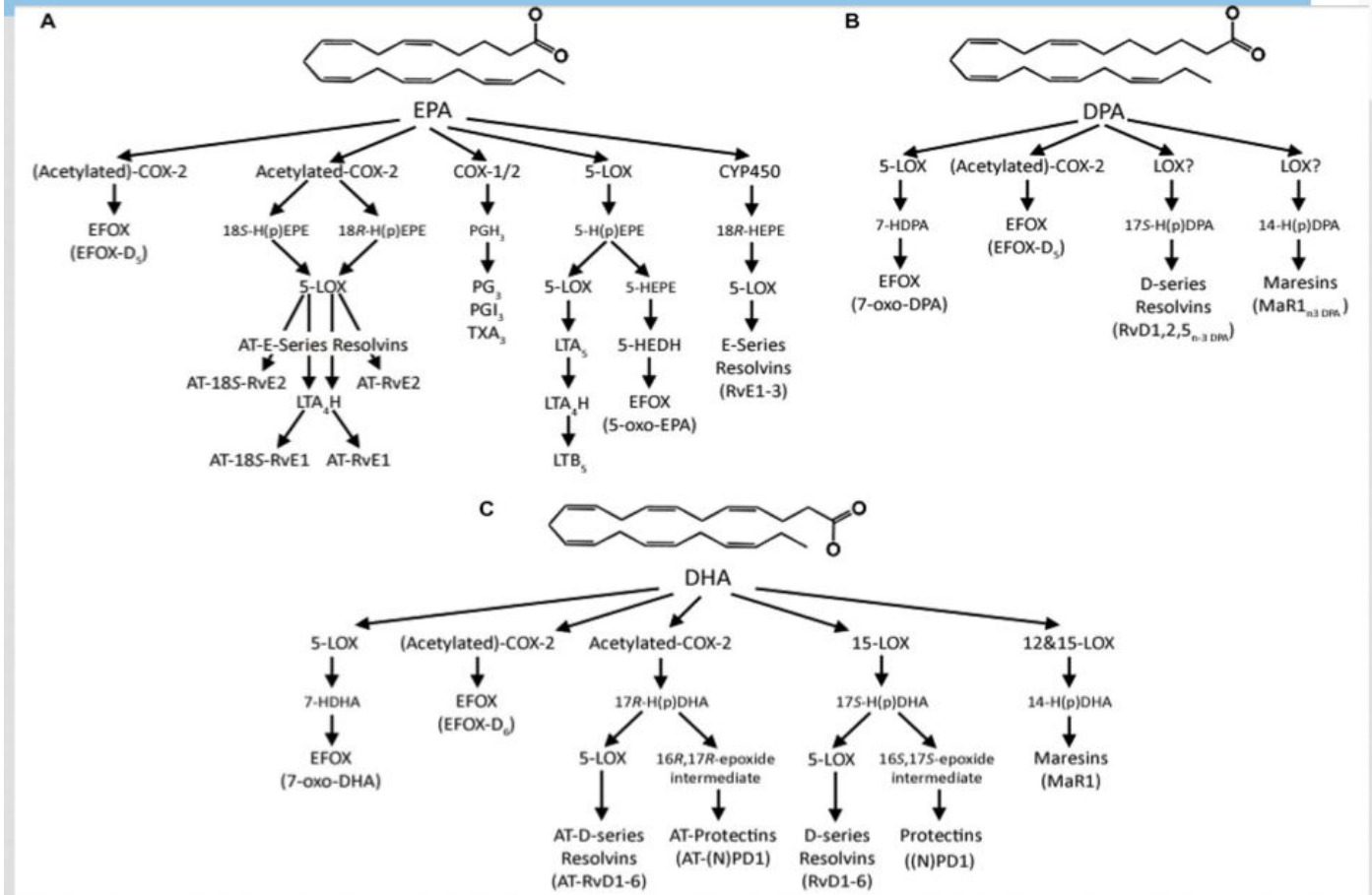
Resolution

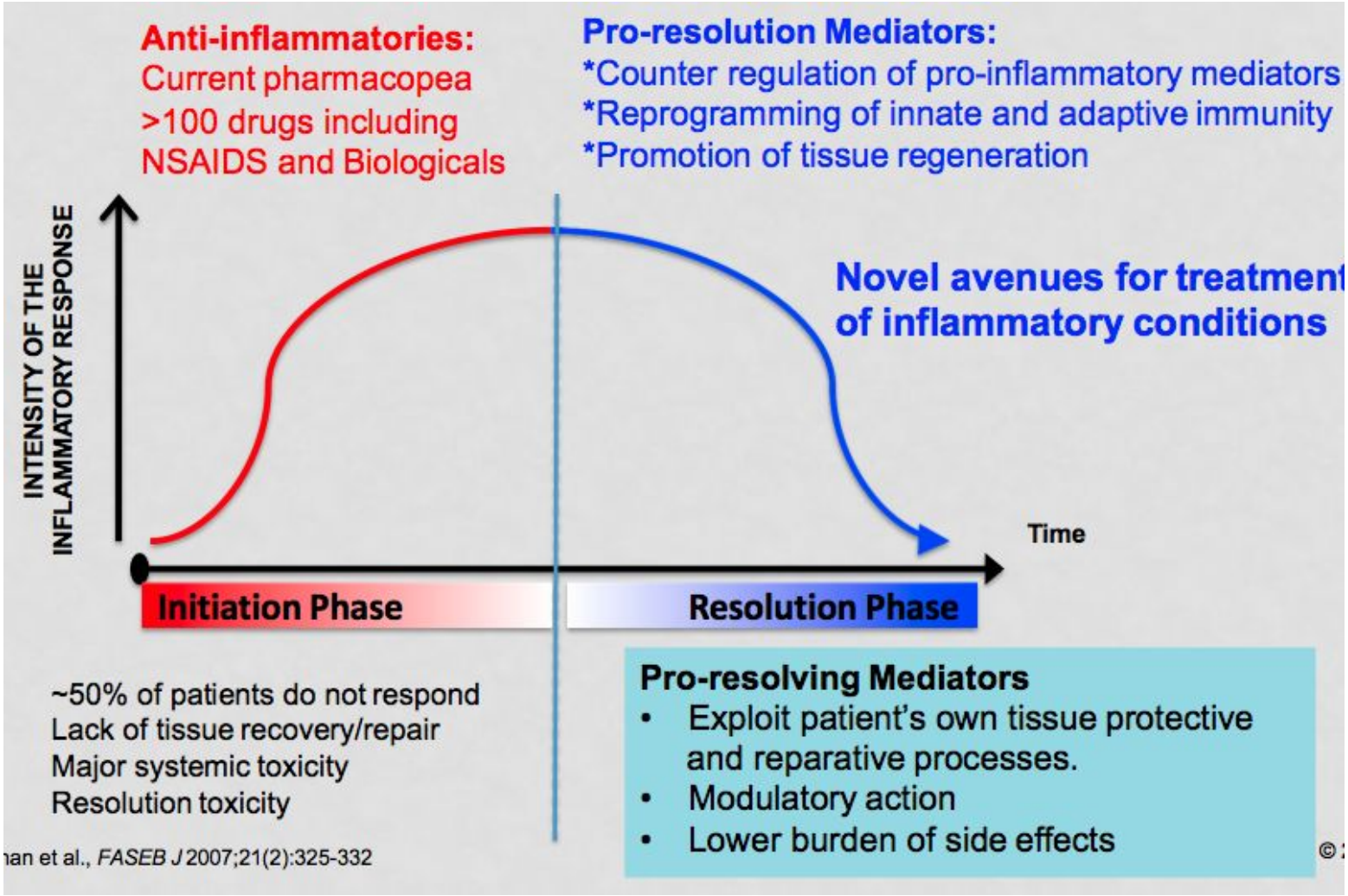
- Removal of microbes, dead cells and debris
- Restoration of vascular integrity and perfusion
- Regeneration of tissue
- Remission of fever
- Relief of pain



Trends in Pharmacological Sciences

RPM'S


A
EPA
(Acetylated)-COX-2
Acetylated-COX-2
COX-1/2
5-LOX
CYP450
EFOX
(EFOX-D3)
18S-H(p)EPE
18R-H(p)EPE
PGH3
5-H(p)EPE
18R-HEPE
5-LOX
PG3
PGI3
TXA3
5-LOX
5-HEPE
5-LOX
AT-E-Series Resolvins
LTA5
5-HEDH
E-Series
Resolvins
(RvE1-3)
AT-18S-RvE2
AT-RvE2
LTA4H
LTA4H
EFOX
(5-oxo-EPA)
AT-18S-RvE1
AT-RvE1
LTB5
B
DPA
5-LOX
(Acetylated)-COX-2
LOX?
LOX?
7-HDPA
EFOX
(EFOX-D5)
17S-H(p)DPA
14-H(p)DPA
EFOX
(7-oxo-DPA)
D-series
Resolvins
(RvD1,2,5n-3 DPA)
Maresins
(MaR1n3 DPA)
C
DHA
5-LOX
(Acetylated)-COX-2
Acetylated-COX-2
15-LOX
12&15-LOX
7-HDHA
EFOX
(EFOX-D6)
17R-H(p)DHA
17S-H(p)DHA
14-H(p)DHA
EFOX
(7-oxo-DHA)
5-LOX
16R,17R-epoxide
intermediate
5-LOX
16S,17S-epoxide
intermediate
Maresins
(MaR1)
AT-D-series
Resolvins
(AT-RvD1-6)
AT-Protectins
(AT-(N)PD1)
D-series
Resolvins
(RvD1-6)
Protectins
((N)PD1)


Anti-inflammatories:
Current pharmacopea
>100 drugs including
NSAIDS and Biologicals
Pro-resolution Mediators:
*Counter regulation of pro-inflammatory mediators
*Reprogramming of innate and adaptive immunity
*Promotion of tissue regeneration
INTENSITY OF THE INFLAMMATORY RESPONSE
Novel avenues for treatment of inflammatory conditions
Time
Initiation Phase
Resolution Phase
~50% of patients do not respond
Lack of tissue recovery/repair
Major systemic toxicity
Resolution toxicity
Pro-resolving Mediators
• Exploit patient's own tissue protective and reparative processes.
• Modulatory action
• Lower burden of side effects
han et al., FASEB J 2007;21(2):325-332

Interaction of inflammation with pain pathway

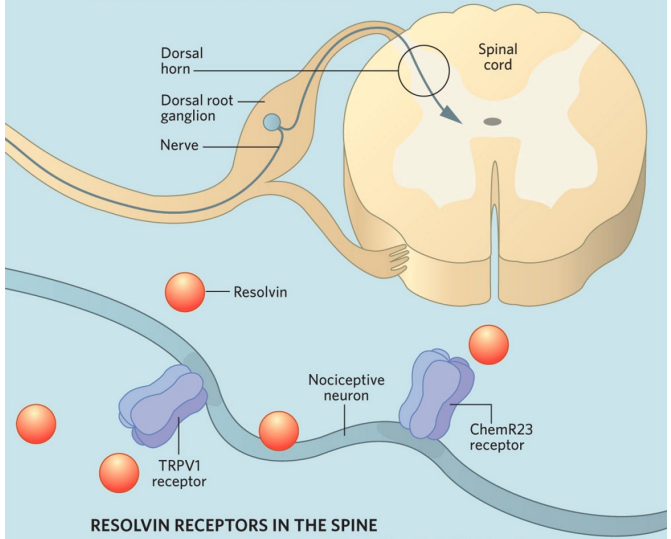
Chronic inflammation increases pain sensitization

- Inflammatory mediators interact with components of the pain pathway
  - nociceptors, peripheral nerves, dorsal root ganglion, neurons in spinal cord
  - facilitates transmission of pain signals through nervous system
  - causes sensitization & leads to chronic pain
- Resolvins can prevent pain sensitization
  - interact directly with pain receptors
  - dampen certain mechanisms of nerve transmission at peripheral nerves and in spine
  - can prevent pain becoming chronic by blocking ‘pain memory’

LUCY READING-IKKANDA FOR THE SCIENTIST, JANUARY 2012

RESOLVINS IN CHRONIC PAIN

Chronic pain is a complicated disorder that can be influenced as much by mood and personal experience as it can by persistent inflammation or unresolved pain. In some cases when pain is constantly relayed through the peripheral nerves to the central nervous system, a sort of imprint or pain memory is created, leading to chronic pain. Resolvins can dampen the nerve transmission that leads to chronic pain by acting both at the peripheral nerve and in the spine.

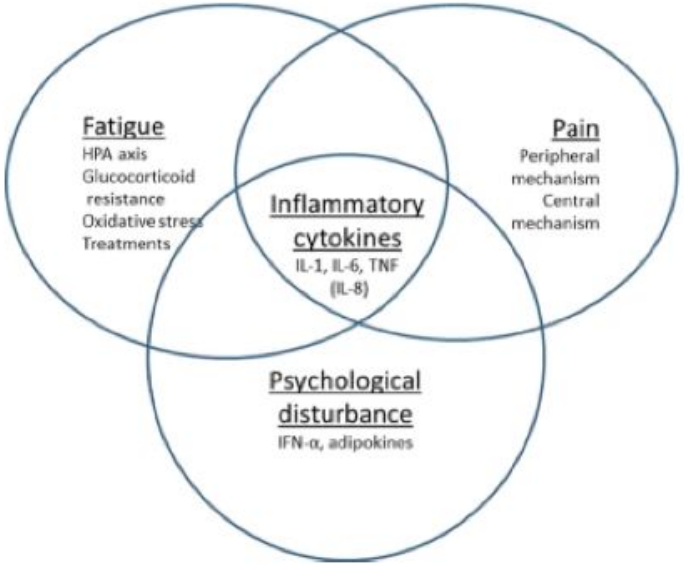


RESOLVIN RECEPTORS IN THE SPINE

Resolvins have been shown to act by indirectly inhibiting the capsaicin receptors called transient receptor potential vanilloid 1 (TRPV1). But they may also reduce inflammation by acting on the ChemR23 receptor, which is expressed along with the TRPV1 receptor on the dorsal horn of the spinal cord. Although it is unclear exactly how the ChemR23 receptor interacts with the TRPV pathway, it appears to be important for the pain-relieving activity of resolvin E1 by blocking the signaling protein ERK.

Chronic inflammation links pain, fatigue & depression

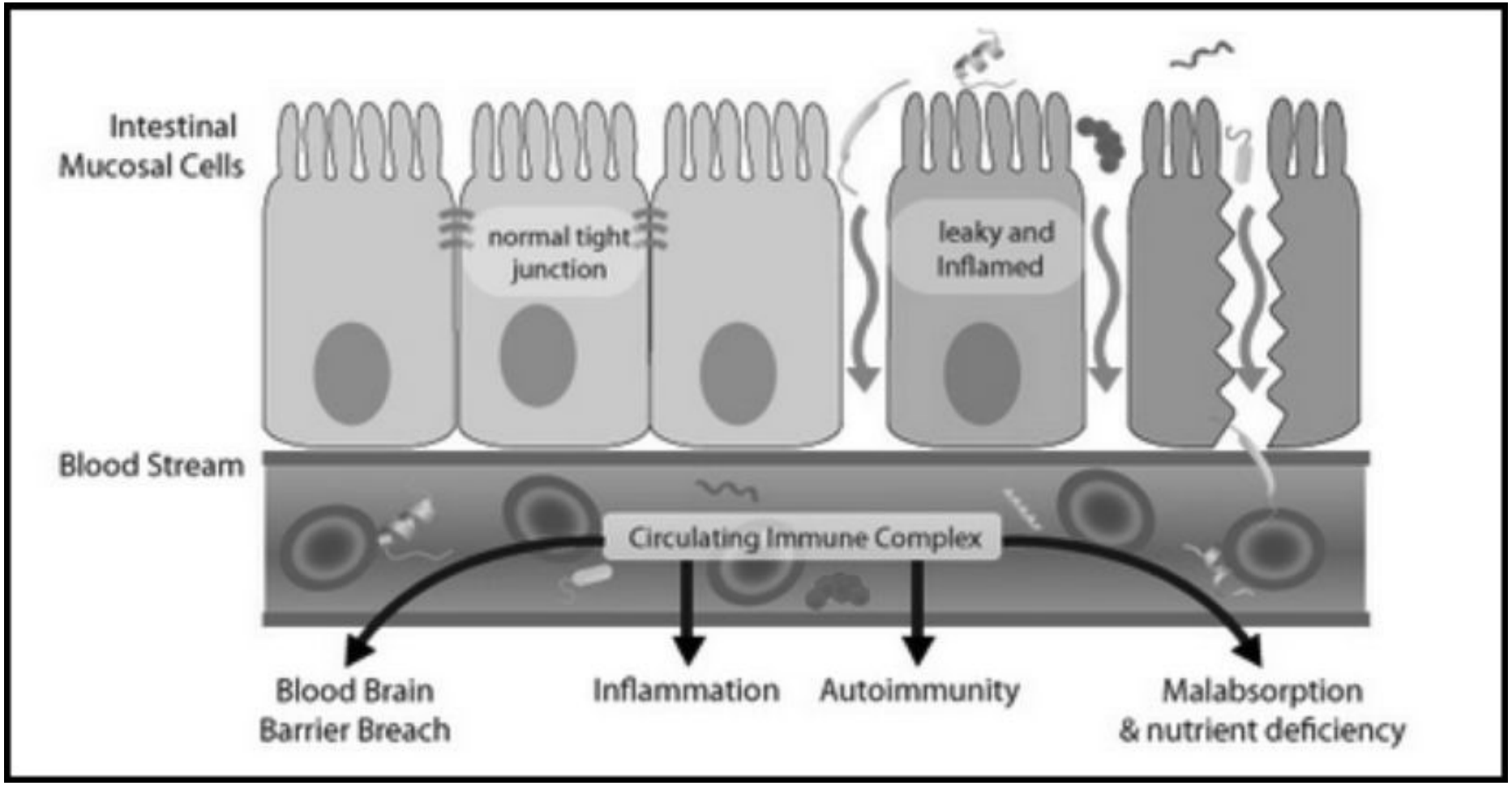
- Chronic inflammation now recognized as common link between pain, fatigue & depression in chronic disease
  - Inflammatory cytokines are associated with all three
  - Resolving chronic inflammation can improve fatigue, pain & mental health



Importance of leaky gut in chronic inflammation

“All Disease Begins in The Gut” - Hippocrates (400 BC)

- genes & environmental triggers interact via breach in intestinal barrier to produce inflammation & autoimmunity
- Dysbiosis - disruption of the gut microbiome
    - poor diet, over-medication, chronic stress, environmental toxins, birth circumstances
- Associated with increased intestinal permeability ‘leaky gut’
    - Increasingly recognized as central mechanism causing chronic inflammation
        - bacterial endotoxins & other molecules leak through compromised barrier
        - enter bloodstream where immune system mounts attack
        - results in a chronic inflammatory response
        - cause of autoimmune conditions, skin conditions, brain disorders
            - “Fire in the gut, fire in the brain”


Intestinal
Mucosal Cells
normal tight
junction
leaky and
Inflamed
Blood Stream
Circulating Immune Complex
Blood Brain
Barrier Breach
Inflammation
Autoimmunity
Malabsorption
& nutrient deficiency

Control of chronic inflammation is crucial for health

- Four pillars of health
  - nutrition
  - sleep
  - physical activity
  - stress management


HEALTH BEHAVIORS
SPIRIT & SOUL
DAILY RHYTHM & BALANCE
MOVEMENT EXERCISE & PLAY
FOOD & NOURISHMENT
ENVIRONMENT
SLEEP & REST
RELATIONSHIPS & COMMUNITY
MIND-BODY CONNECTION
COMPASSIONATE
SELF
AWARENESS
Prevention, Medical, and Wellness Care


The Pfizer Circle of Hell
ZARONTIN
(to treat seizures)
Side Effects May Include:
Hiccups
Urticaria
Myopia
Night terrors
Diarrhea
LOMOTIL
(to treat diarrhea)
Side Effects May Include:
Pancreatitis
Swollen gums
Confusion
Anorexia
Depression
ZOLOFT
(to treat depression)
Side Effects May Include:
Abnormal bleeding
Nausea
Insomnia
Constipation
Impotence
VIAGRA
(to treat impotence)
Side Effects May Include:
Headaches
Dyspepsia
Impaired vision, such as cyanopsia, seeing everything in blue
Abnormal heart rate
CALAN
(to treat abnormal heart rate)
Side Effects May Include:
Constipation
Hair loss
Increased urination
Hypotension
Psychotic disorder
NAVANE
(to treat psychotic disorder)
Side Effects May Include:
Blurred vision
Insomnia
Tachycardia
Abnormal contraction of muscles
Seizures
SEIZURES
DIARRHEA
DEPRESSION
IMPOTENCE
ABNORMAL HEART RATE
PSYCHOTIC DISORDER

Anti-inflammatory diets

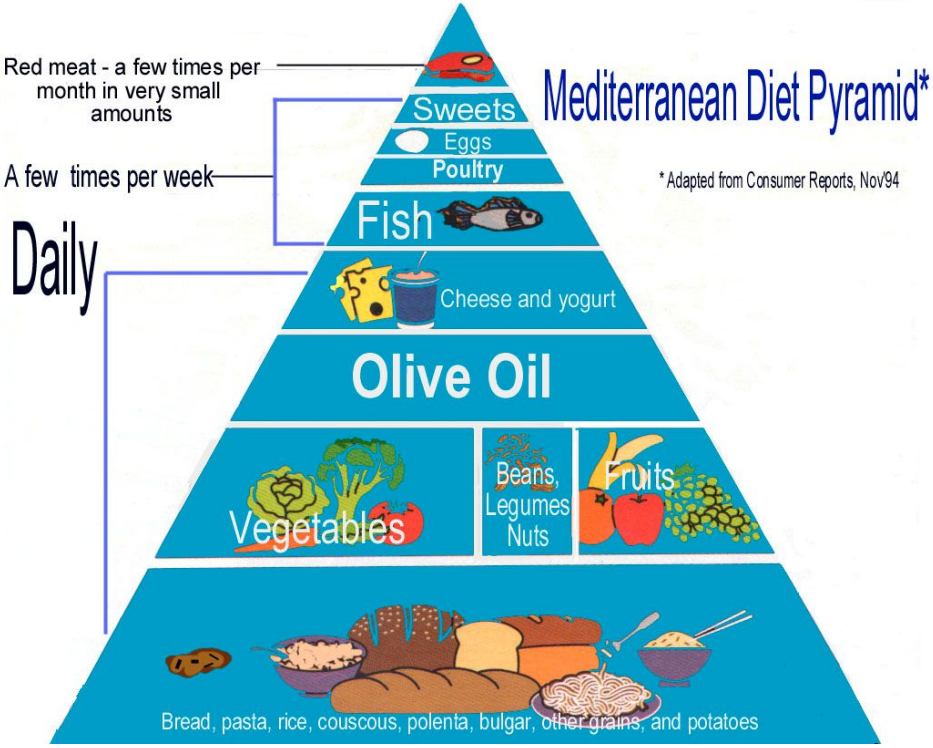
Reduce inflammation by:

- Removing dietary inflammation triggers
  - ‘sugar/fructose, wheat & industrial seed oils
  - dairy, grains, legumes, processed foods, alcohol
  - any food to which you have an allergy or sensitivity
- Increasing intake of anti-inflammatory / pro-resolving foods & herbs
  - high ratio of omega-3 (anti-inflammatory/pro-resolving) to omega-6 (pro-inflammatory)
  - antioxidant rich = “eat the rainbow”
- Balancing blood sugar
  - low glycaemic load foods
- Improving gut environment
  - reduce excess permeability
  - boost beneficial microflora

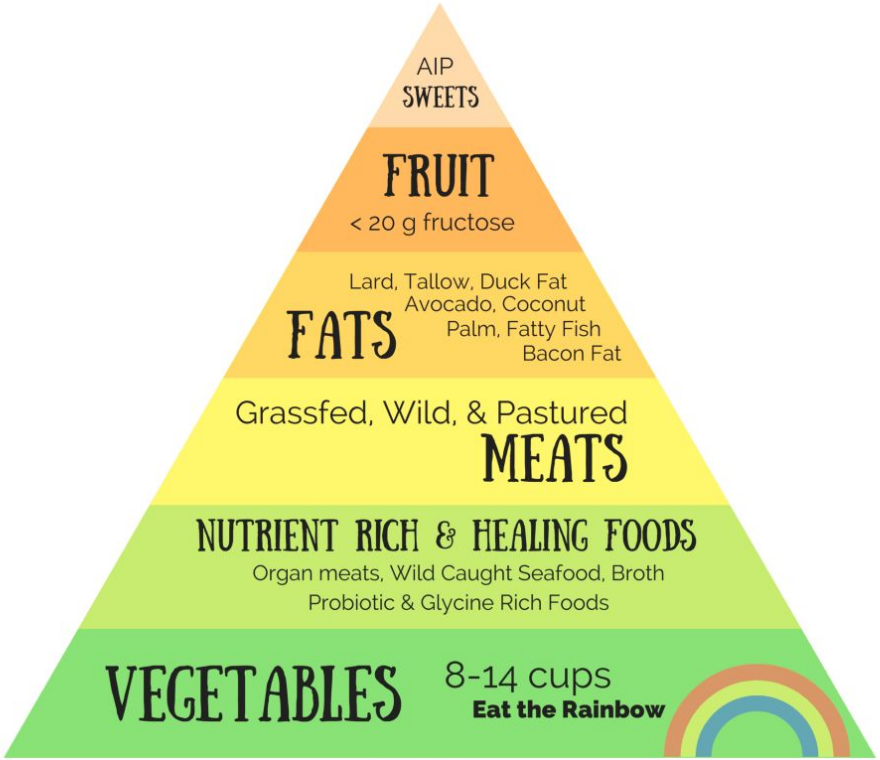
Anti-inflammatory diets

Adopt an anti-inflammatory diet **that works for your specific genetic/metabolic needs**

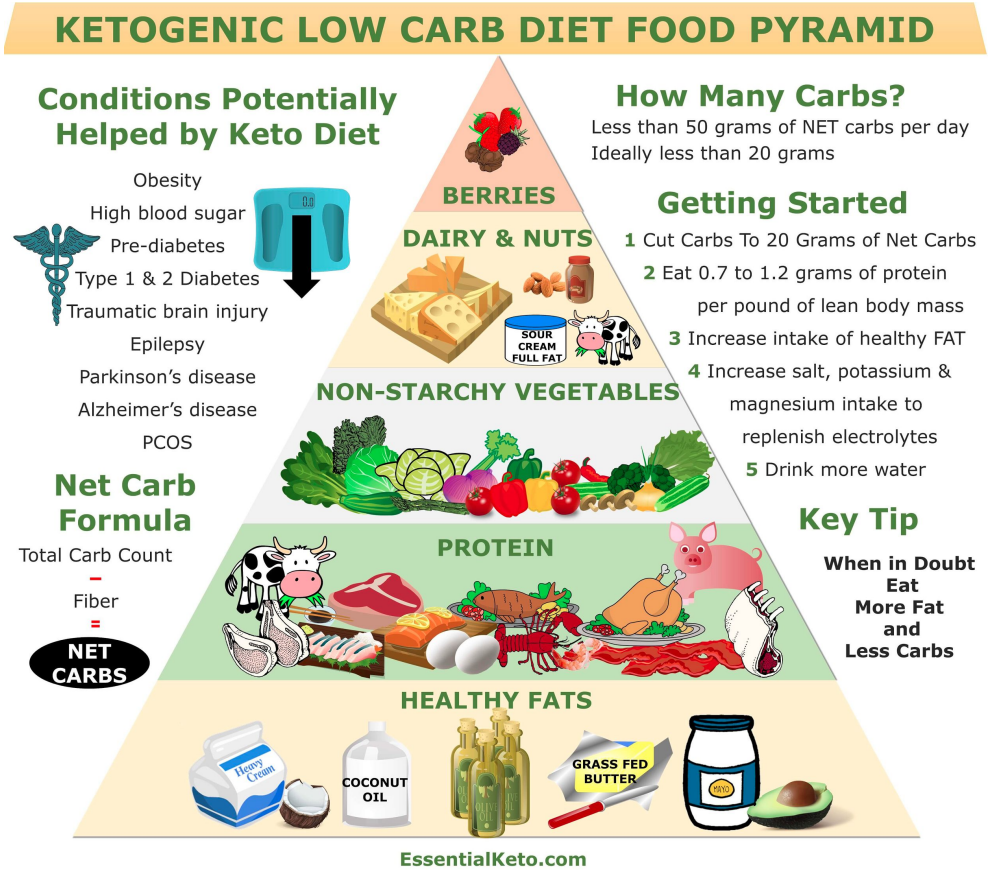
- Mediterranean diet (most studied)
- Anti-inflammatory diet (Dr Andrew Weil)
- Low-carb diets
  - paleo diet & autoimmune paleo protocol (Chris Kresser)
  - ketogenic diet (high fat, very low carb)
  - low-FODMAP diet (low in fermentable oligosaccharides, disaccharides, monosaccharides, polyols)
- Caloric restriction
  - intermittent fasting
- GAPS (Gut and Psychology Syndrome) diet


Red meat - a few times per month in very small amounts
A few times per week
Daily
Mediterranean Diet Pyramid*
* Adapted from Consumer Reports, Nov'94
Sweets
Eggs
Poultry
Fish
Cheese and yogurt
Olive Oil
Vegetables
Beans, Legumes Nuts
Fruits
Bread, pasta, rice, couscous, polenta, bulgar, other grains, and potatoes


Dr. Weil's Anti-Inflammatory Food Pyramid
HEALTHY SWEETS (such as plain dark chocolate) Sparingly
RED WINE (optional) No more than 1-2 glasses a day
SUPPLEMENTS Daily
TEA (white, green, oolong) 2-4 cups a day
HEALTHY HERBS & SPICES (such as garlic, ginger, turmeric, cinnamon) Unlimited amounts
OTHER SOURCES OF PROTEIN (dairy [natural cheeses, yogurt], omega-3 enriched eggs, skinless poultry, lean meats) 1-2 a week
COOKED ASIAN MUSHROOMS Unlimited amounts
WHOLE-SOY FOODS (edamame, soy nuts, soymilk, tofu, tempeh) 1-2 a day
FISH & SHELLFISH (wild Alaskan salmon, Alaskan black cod, sardines) 2-6 a week
HEALTHY FATS (extra-virgin olive oil, nuts - especially walnuts, avocados, seeds - including hemp seeds and freshly ground flaxseeds) 5-7 a day
WHOLE & CRACKED GRAINS 3-5 a day
PASTA (al dente) 2-3 a week
BEANS & LEGUMES 1-2 a day
VEGETABLES (both raw and cooked, from all parts of the color spectrum, organic when possible) 4-5 a day minimum
FRUITS (fresh in season or frozen, organic when possible) 3-4 a day



AIP FOOD PYRAMID



Anti-inflammatory lifestyle

- Exercise regularly
  - individual bouts of exercise tend to promote acute inflammation
    - microinjury to muscle tissue stimulates muscle growth
  - however when done regularly over the long term, it prevents chronic inflammation
  - oxidative stress from exercise forces body to build up antioxidant defenses.
  - extended exercise programs help reduce inflammatory markers
- Maintain a healthy weight
  - fat cells can initiate inflammatory reaction
    - act like immune cells - releasing pro-inflammatory cytokines
- Sit for less than three hours a day
  - chronic sitting is an independent risk factor for mortality
  - take movement/stretch breaks & use a standing desk

Anti-inflammatory lifestyle

- Stretch
  - yoga, tai Chi decrease levels of circulating pro-inflammatory cytokines
  - stretching connective tissue activates local pro-resolving mechanisms
  - increases resolvin production
- Get enough good quality sleep
  - insomnia & circadian rhythm disruption are pro-inflammatory
- Reduce stress
  - stress & anxiety are pro-inflammatory
  - body interprets these emotions as being under attack no matter what their cause
  - raises cortisol & releases inflammatory mediators throughout body

Anti-inflammatory lifestyle

- Meditate
  - reduces biomarkers of inflammation
  - dampens activity of genes associated with inflammation
  - essentially reversing molecular damage caused by stress
- Avoid exposure to pesticides and other toxic chemicals
  - cause inflammation
  - disrupt gut flora
- Brush and floss teeth regularly
  - periodontal disease has been linked to chronic inflammation, heart disease & Alzheimer’s

Basic anti-inflammatory/pro-resolving supplement stack

- Each supplement helps reduce inflammation by a bit in its own way
- Taken additively, as a 'stack' over time, can approach effect level of medications (NSAIDs & steroids)
- Typical stack = omega-3 oil + enzymes + herbal formula

Basic anti-inflammatory/pro-resolving supplement stack

Omega-3 oil

- Omega-3 fatty acids are essential for resolving inflammation.
- Barlean's Fish Oil Omega Swirl Ultra High Potency (delicious, tastes like dessert!)
    - take 1-2 tablespoons per day for a therapeutic dose

Enzymes

- Pure Encapsulations Systemic Enzyme Complex (contains bromelain & other anti-inflammatory enzymes)
    - promotes connective tissue healing. Supports muscle, joint and connective tissue health.
        - http://www.pureencapsulations.com/systemic-enzyme-complex.html
- Bromelgin **(**high dose bromelain plus herbs)
    - proteolytic enzyme plus Chinese herbs, both with anti-inflammatory actions
        - https://www.goldenneedleonline.com/Bromelgin.html

Basic anti-inflammatory/pro-resolving supplement stack

Herbal anti-inflammatories

- Pure Encapsulations CurcumAsorb (highly bioavailable turmeric/curcumin extract)
  - http://www.pureencapsulations.com/curcumasorb.html
- Pure Encapsulations Boswellia AKBA (highly bioavailable frankincense/boswellia extract)
  - http://www.pureencapsulations.com/boswellia-akba.html
- New Chapter Zyflamend (general herbal anti-inflammatory with multiple ingredients)
  - http://www.newchapter.com/zyflamend/zyflamend-whole-body

Vitamin D

- get tested - If your 25(OH)D level is less than 20 ng/mL
  - you likely need some combination of UV exposure, cod liver oil & vitamin D supplement