INFLAMMATION

- a fire within *(“festering”)*

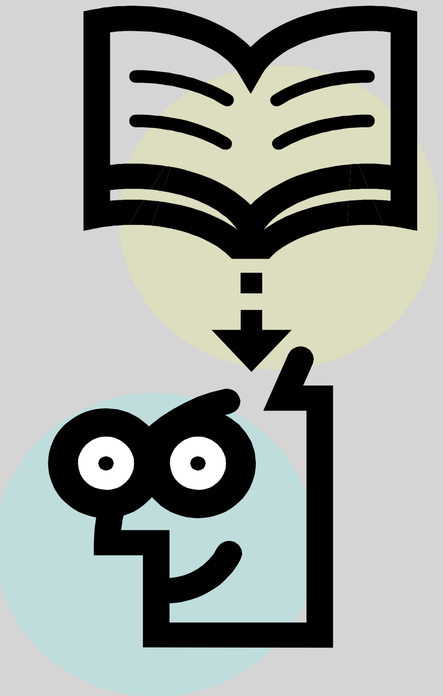
INFLAMMATION *

- fr. Latin word: *in* + *flammō* + *tiō* *
  - meaning the act of setting ablaze, or the act of setting aflame

Objectives:

We do this lecture so that:

- We will have an intelligent grasp of what inflammation is, and
- We will learn how to reduce the risks of developing inflammation.



Introduction:

- **INFLAMMATION** is the body's response to tissue injury be it from:
  - microbial infection,
  - chemical irritants,
  - nutritional imbalance,
  - lack of oxygen,
  - Immune response,
  - physical agents like:
    - extreme temperatures,
    - extreme pressure, or
    - ionizing radiation.

Why is inflammation necessary

- **FUNCTION:**
  - Gets rid of irritating stimuli at the site of injury so that it doesn’t spread,
  - It manages to clear dead cells and other tissue substances at the site of injury,
  - It starts the repair process at the site of injury.

IMMUNITY: Innate vs. Adaptive

- **IMMUNITY-** is the body's armed forces
  1. **Innate immunity-** that which you are born with; it distinguishes between self and non-self; rapidly fights against anything non-self
  2. **Adaptive immunity-** that which is learned by the immune system; takes time to work and it highly specific

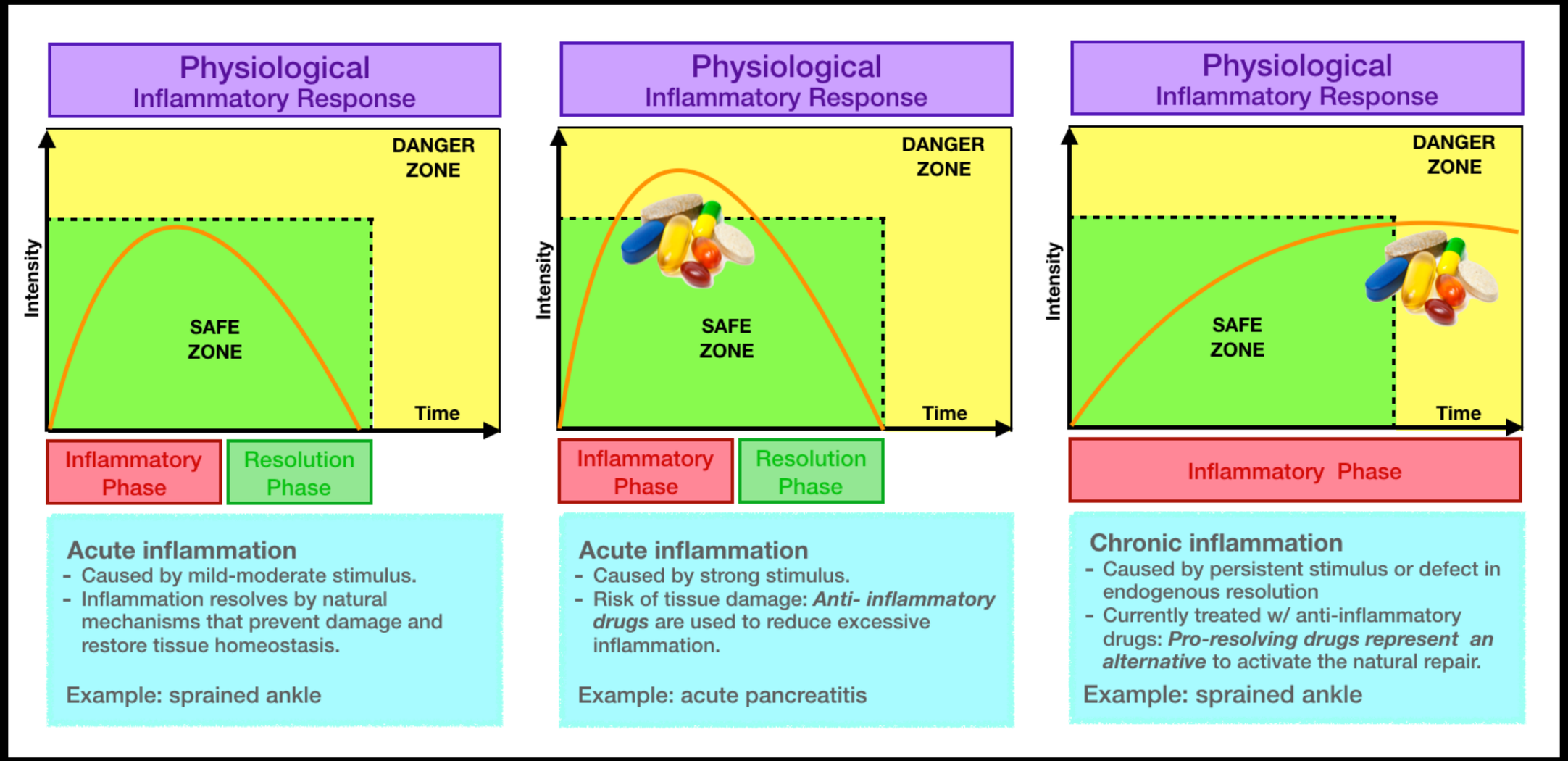
Immunity: Innate vs. Adaptive

Characteristics	Innate Immunity	Adaptive immunity
Presence	Innate immunity is something already present in the body.	Adaptive immunity is created in response to exposure to a foreign substance.
Specificity	Non-Specific; fights any invader	Specific
Response	Rapid	Slow (1-2 weeks)
Potency	Limited and Lower potency	High potency
Inheritance	Immunity is generally inherited from parents and passed to offspring.	Immunity is not passed from the parents to offspring, hence it cannot be inherited.
Memory	Cannot react with equal potency upon repeated exposure to the same pathogen.	Adaptive system can remember the specific pathogens which have encountered before.
Example	White blood cells fighting bacteria, causing redness and swelling, when you have a cut.	Chickenpox vaccination so that we don't get chickenpox because adaptive immunity system has remembered the foreign body.

Acute vs. Chronic Inflammation

FACTORS	ACUTE	CHRONIC
Causative agent	Pathogens, irritants, damage	Persistent acute inflammation due to non-degradable pathogens, persistent foreign bodies, or autoimmune reactions
Onset	Immediate	Delayed
Duration	Few days	Up to months, or years
Specificity	Non-specific	Specific- involves acquired immunity
Major cells	Neutrophils, basophils, eosinophils, monocytes, macrophages	Monocytes, macrophages, lymphocytes (antibodies), plasma cells, fibroblasts
Outcomes	Resolution, abscess formation, and chronic inflammation	Tissue destruction, fibrosis (scarring)

Acute vs. Chronic Inflammation



Resolution in an "over-inflamed era." The Biochemist, vol. 39:4, p. 5. August 2017

INFLAMMATION- Cardinal Signs & Symptoms

1. Heat —> Calor
2. Redness —> Rubor
3. Swelling —> Tumor
4. Pain —> Dolor
5. Functio laesa —> Loss of function

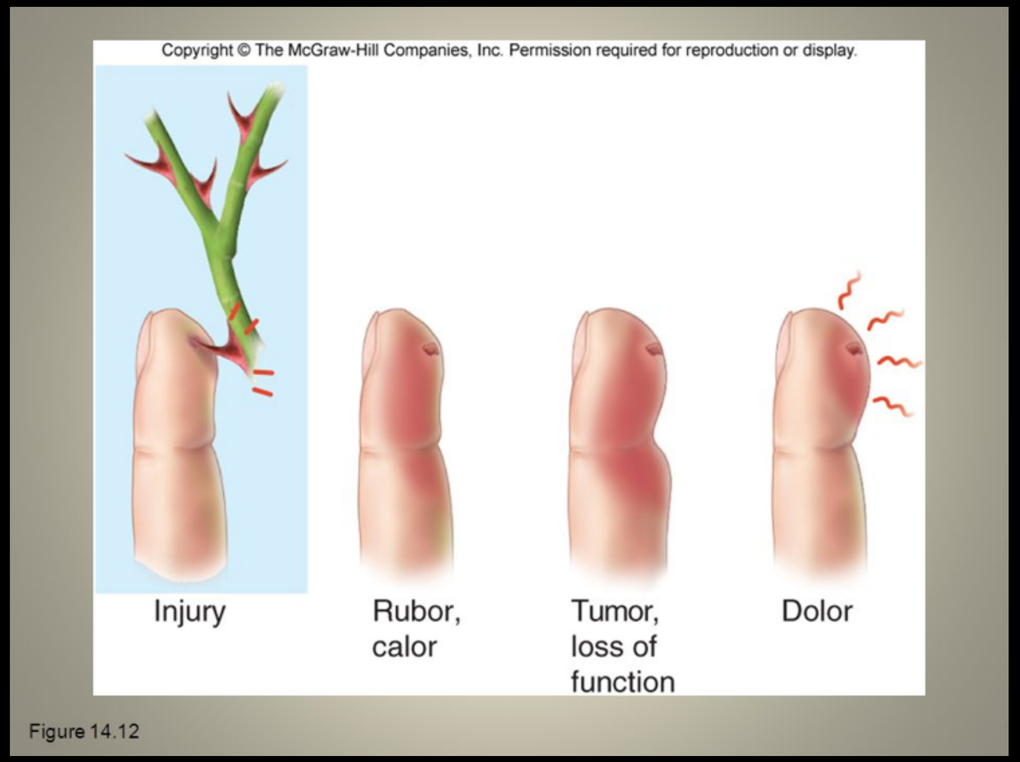
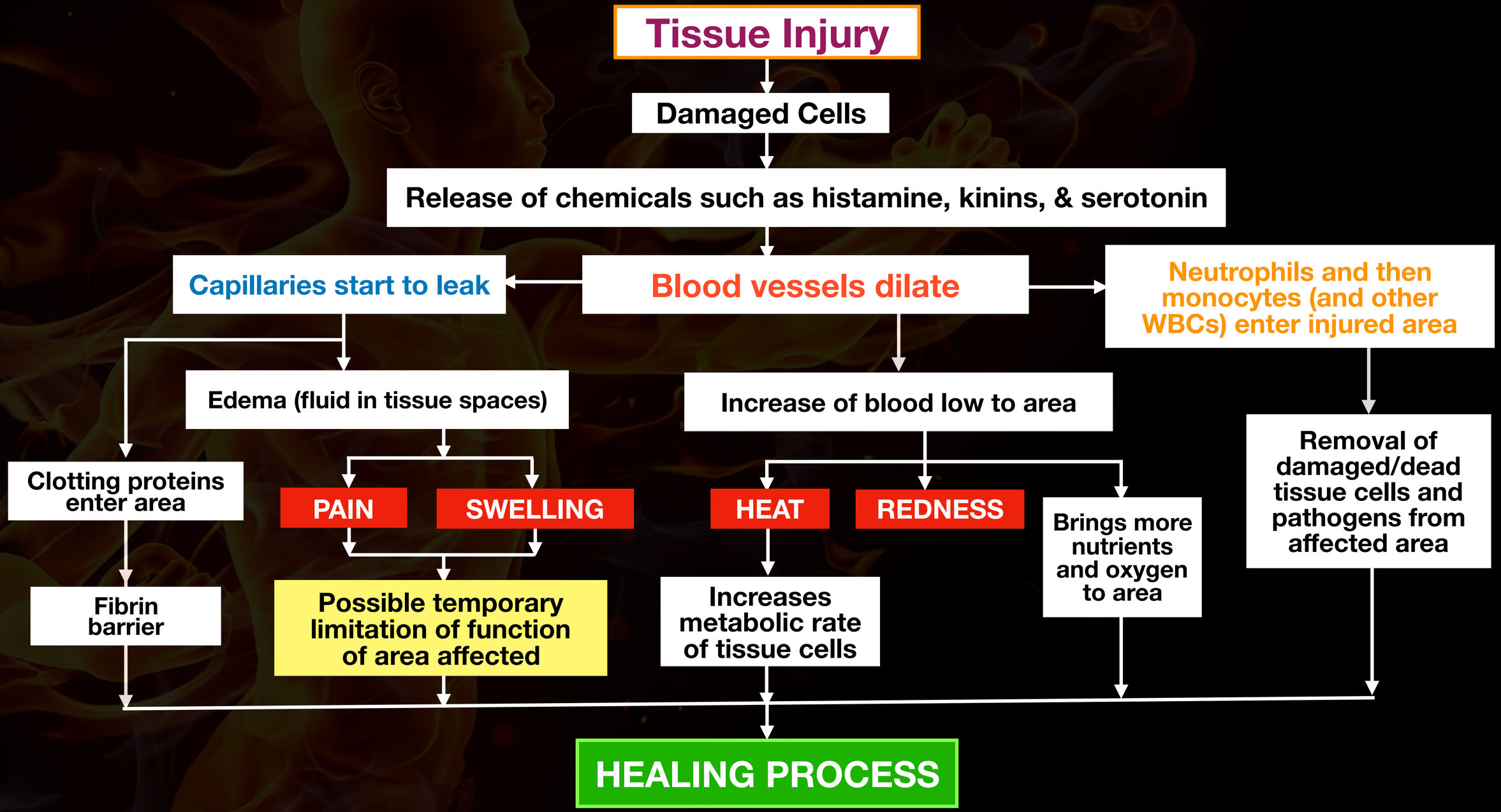
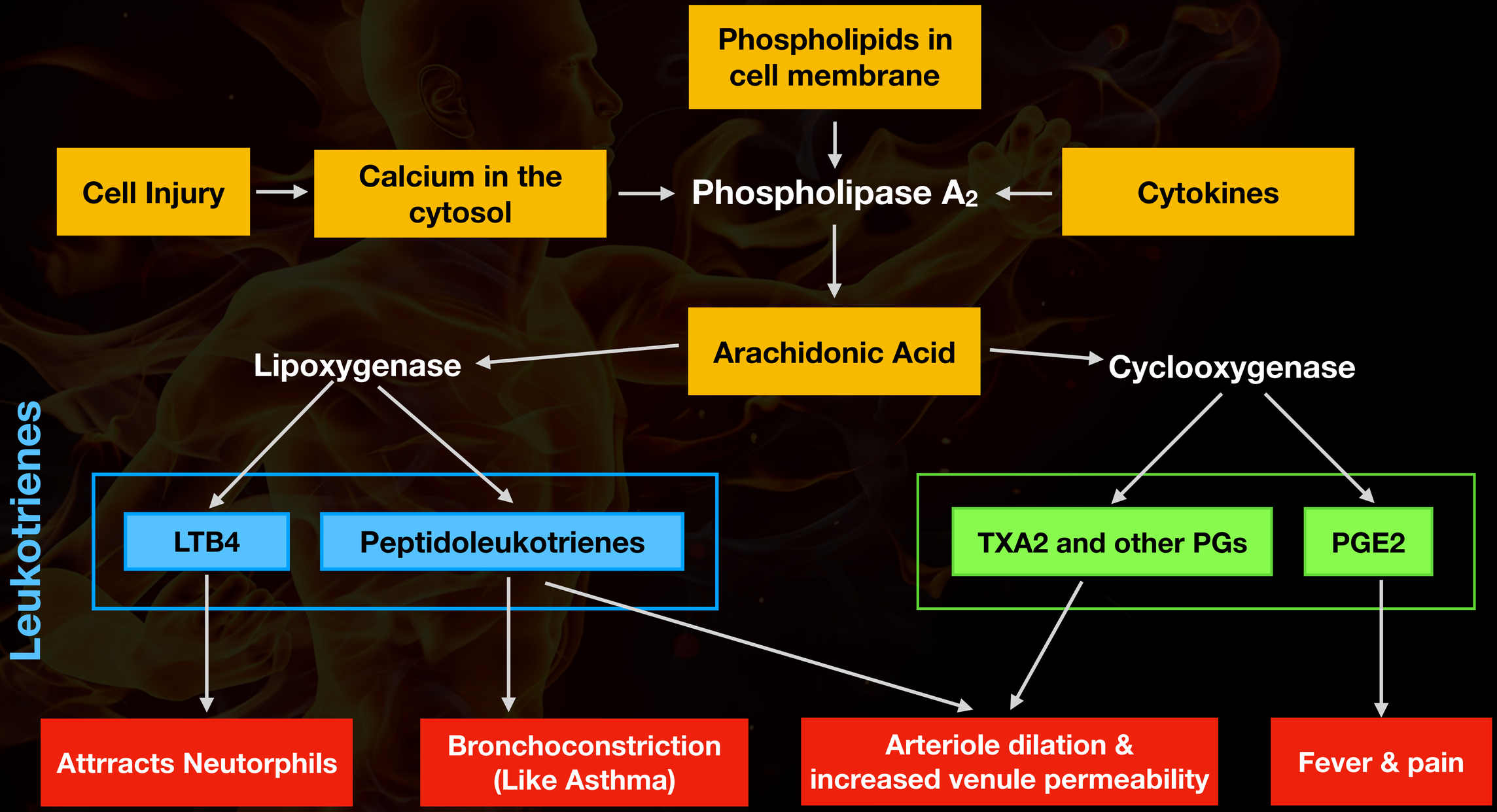


Figure 14.12

Physiology Behind Initial Inflammation



Physiology Behind Initial Inflammation cont.



New Horizons in Inflammation

Cardiovascular Diseases
Atherosclerosis
Heart Failure
Stroke
Hypertension

All Cancer Stages
Initiation
Progression
Metastasis

Pulmonary Diseases
Asthma
COPD
Hay Fever
Bronchitis

Autoimmune Disorders
Inflam. Bowel Dis.
Crohn's Disease
Lupus
Multiple Sclerosis
Type I Diabetes

CHRONIC INFLAMMATION

Diabetic Complications
Neuropathy
Retinopathy
Hypertension
Atherosclerosis
Heart Disease

Bone & Joint Diseases
Osteoarthritis
Rheumatoid Arthritis
Osteopenia
Osteoporosis

Metabolic Disorders
Type II Diabetes
Fatty Liver Disease
Renal Failure

Neurologic Diseases
Depression
Alzheimer's
Parkinson's
Multiple Sclerosis
Autism (?)

Inflammation & Chronic Diseases Pathogenesis

Pathogens Bacteria, Virus, Fungi, Parasites, Chemicals/Toxins, Extreme Temperature, Radiation, etc.

Health Issues HBP, HyGly, CRP, HChol, WGain, LGut, etc.

Biochemical &/or Hormonal Imbalances

Poor Diet & Lifestyle

- "Dead" (Processed) Food*
- Nutrient Deficiencies
- Drug/Medication
- Sedentary Lifestyle
- High Stress, Insomnia
- Medical/Dental Practices

* "Dead" Food include: Breads, Sodas/Bottled juices, Processed Fats, GMOs, Excitotoxins (MSG), Artificial Sweeteners, Alcohol, Caffeine

Immune Response

Acute Inflammation

ROS ⬆
TNF, IL ⬆
Toxicity ⬆
Hormones

Pathogens Killed → **Cells/Tissues Repaired**

Pathogens Not Killed → **Cells/Tissues Not Repaired**

Immune System IMPAIRED ↔ **New Infection**

Oxidative Stress

Chronic Inflammation

ROS

Cell Dysfunction or Damage

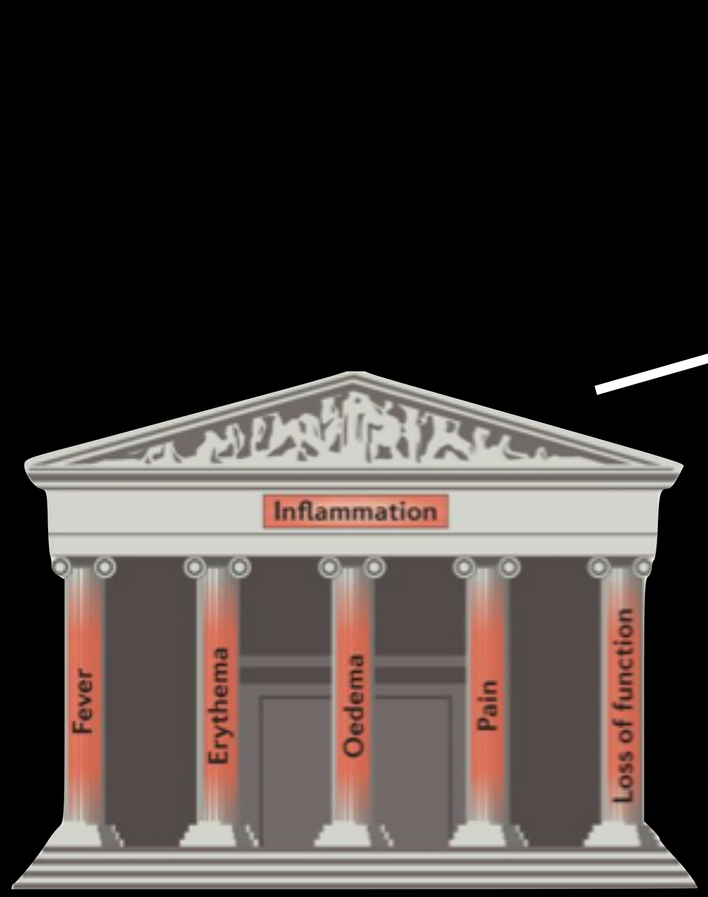
CRP ⬆
IL-6 ⬆
TNF-α ⬆
PV, ESR ⬆

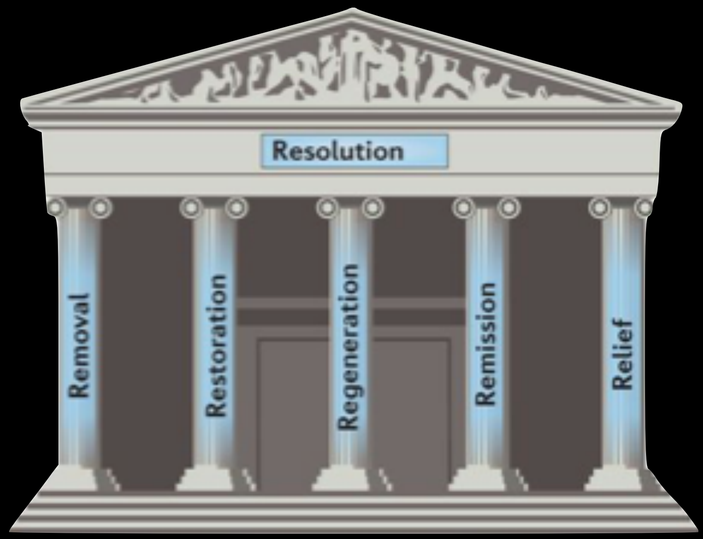
- **Infectious Diseases**
- **Heart Disease**
- **Cancer**
- **Diabetes T2 Complications**
- **Obesity**
- **Alzheimer's Disease**
- **Autoimmune Diseases**

⋮

ETC

Inflammation & Chronic Disease

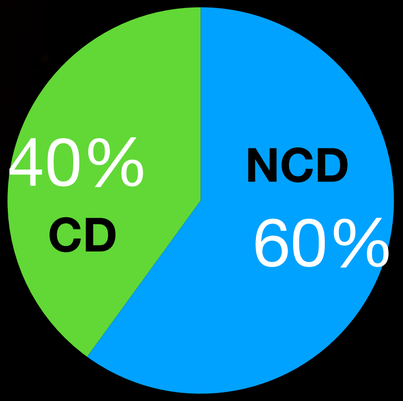




Nature Reviews / Immunology

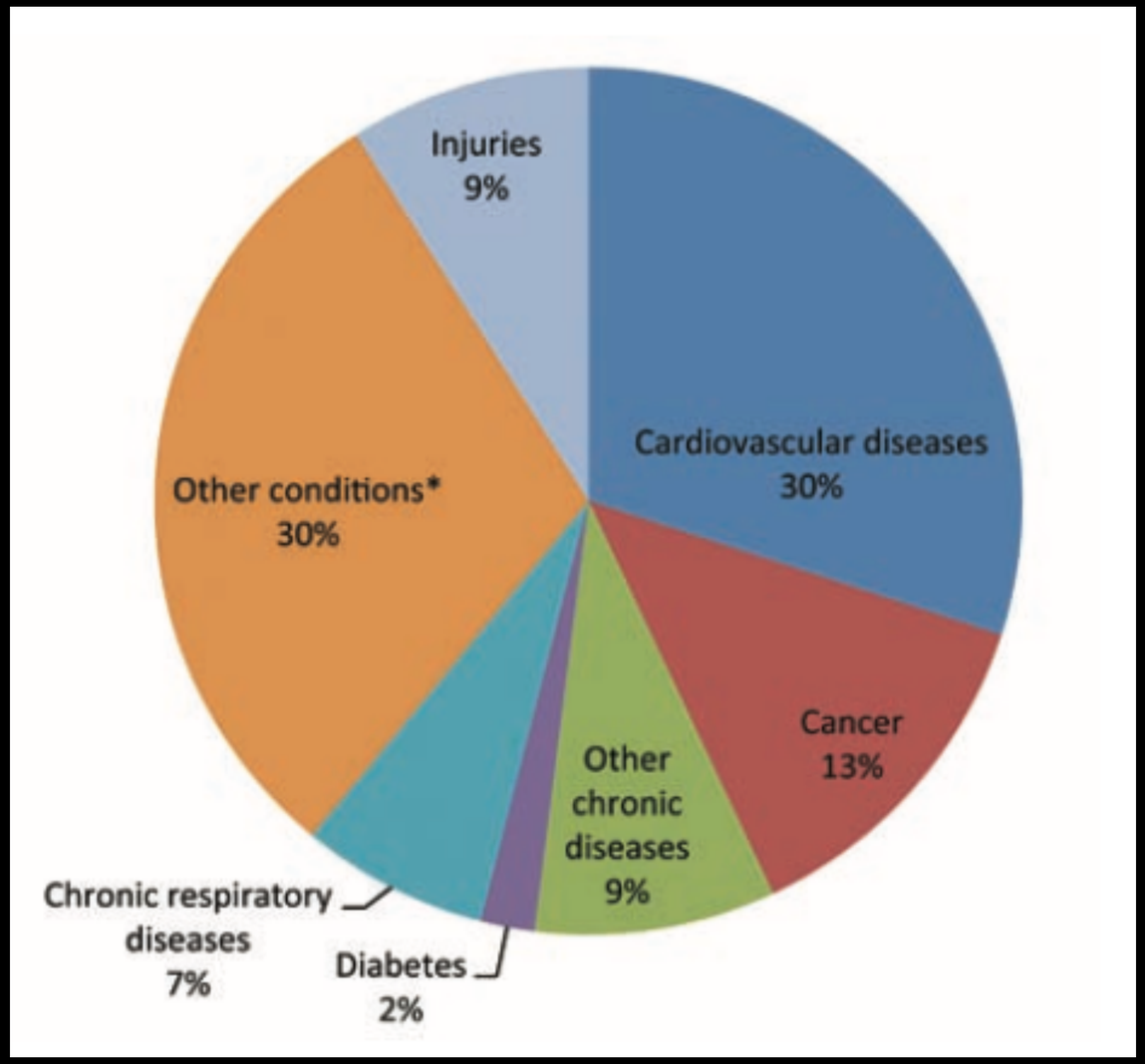
Inflammation & Non-Communicable Diseases (NCD)

- NCDs constitute more than 60% of deaths worldwide
- 25% of NCDs affect ages <60y/o
- NCDs account for 48% of the lost years of healthy life vs. 40% of CDs, maternal / perinatal conditions and nutritional deficiencies and injuries.



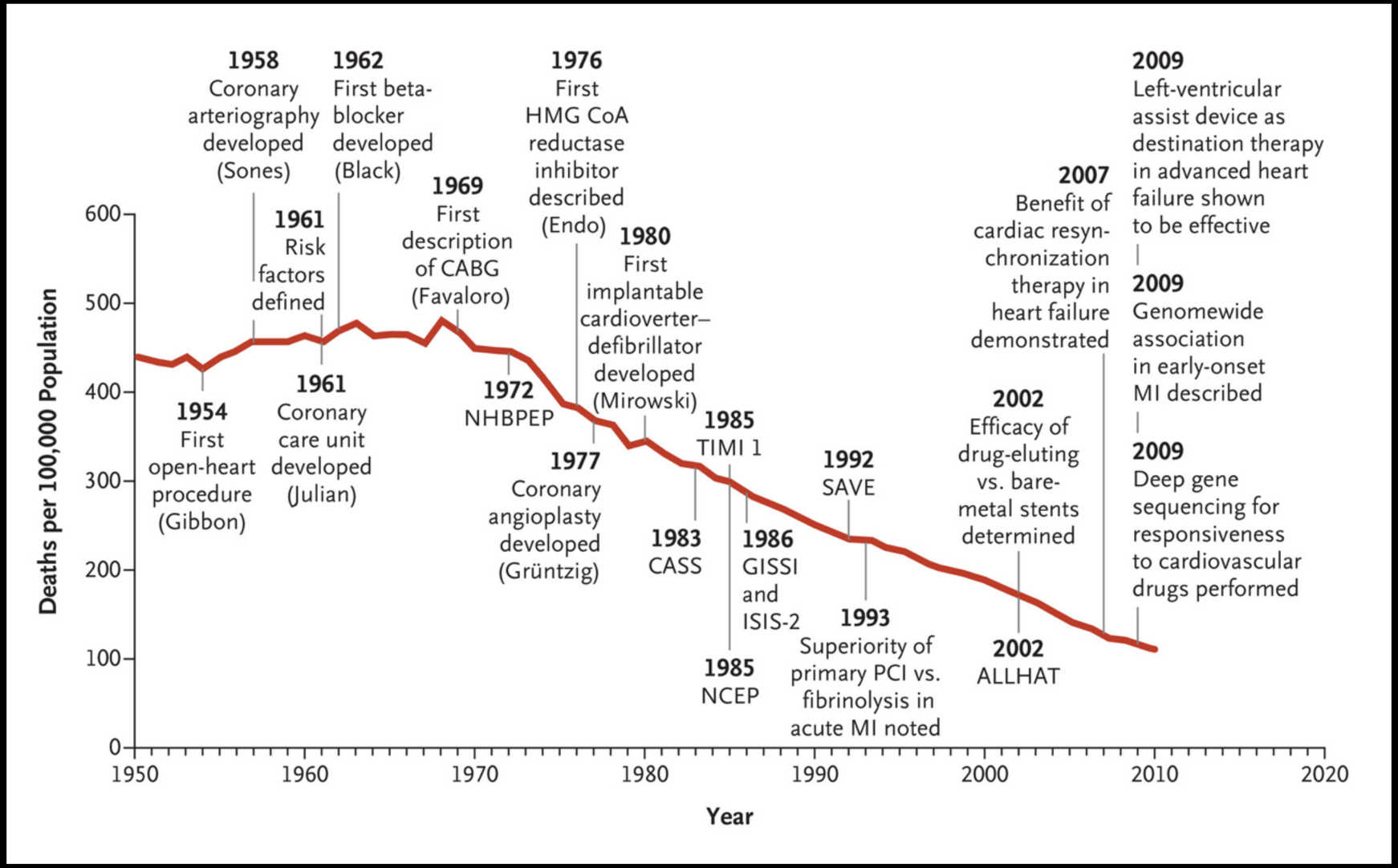
Harvard Med. School “World Economic Forum” Sept 2011

Inflammation & Cardiovascular Disease



Data are for 2005. Source: (WHO, 2005a)

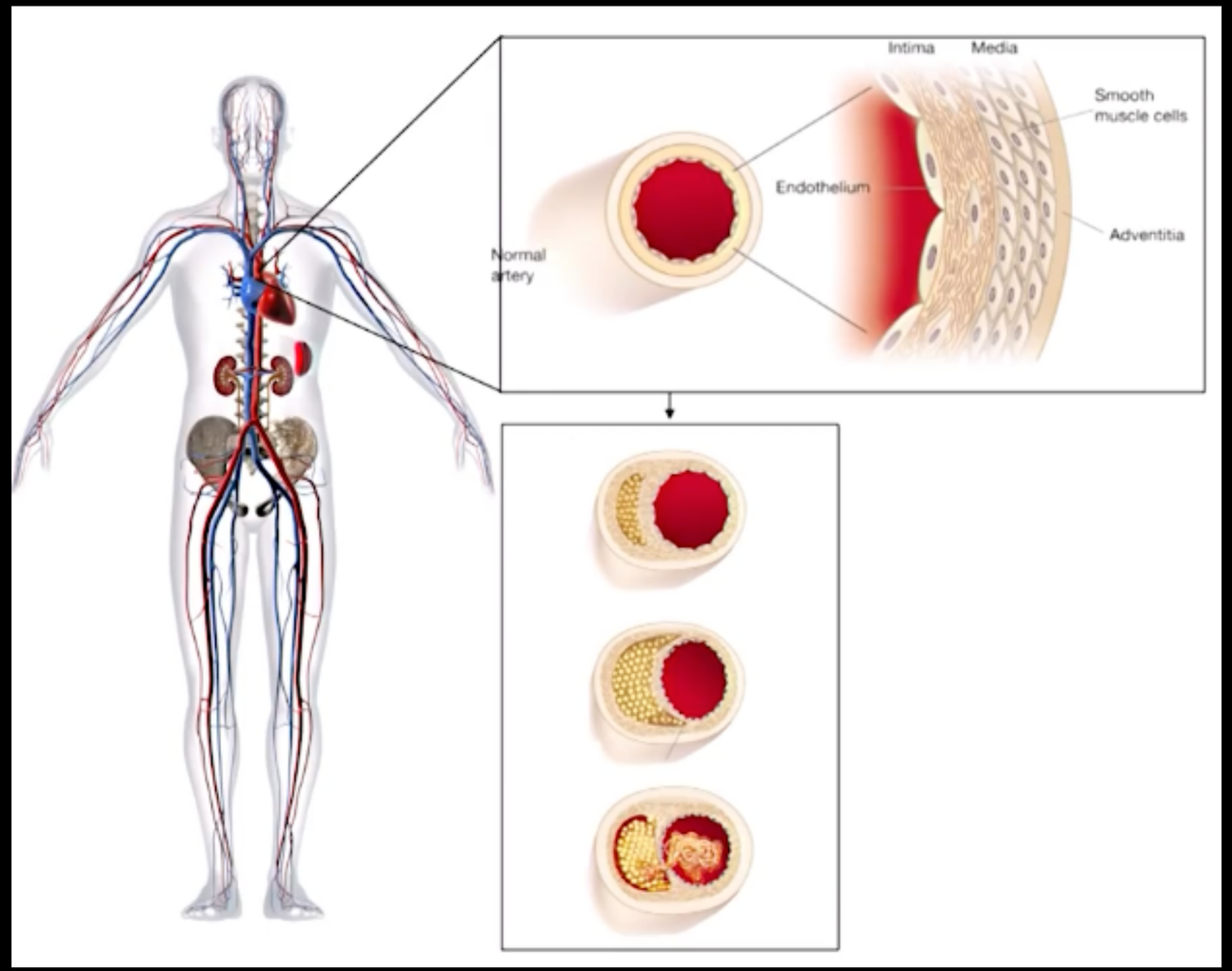
Inflammation & Cardiovascular Disease



Nabel & Braunwald, N Engl J Med 2012; 366:54-63

Inflammation & Cardiovascular Disease

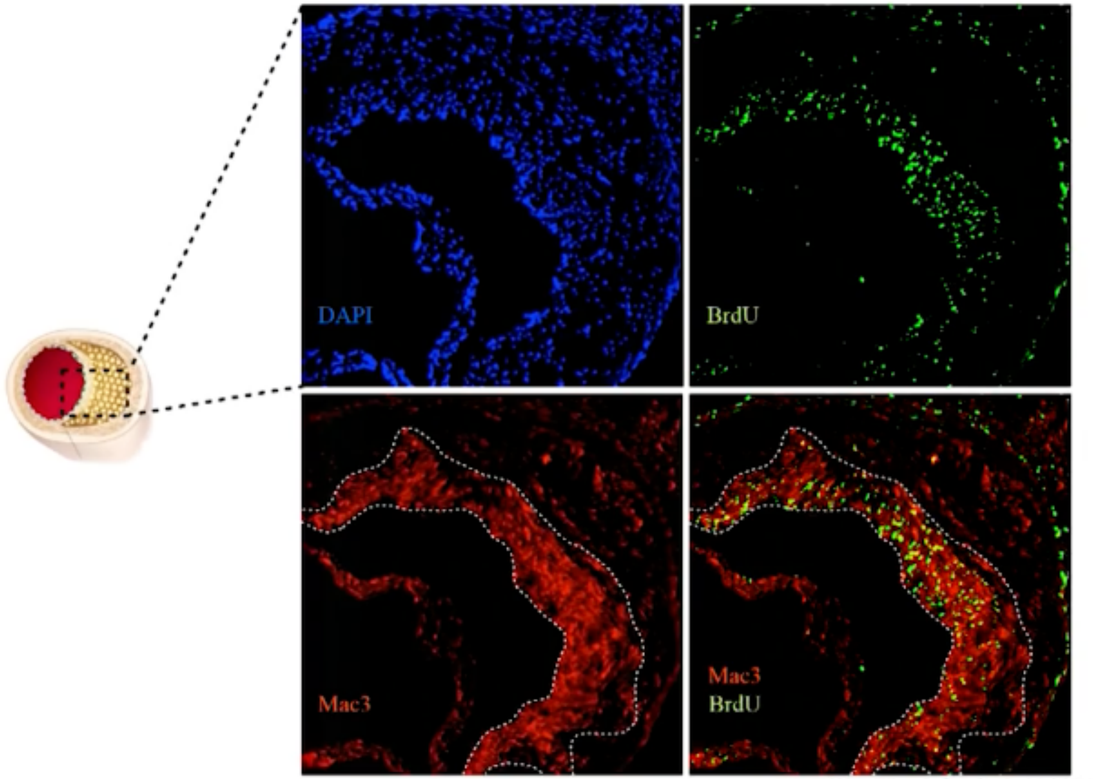
- ATHEROSCLEROSIS- hardening of the blood vessels secondary to accumulation of fat that can cause blockage of blood flow



https://hms.harvard.edu/news-events/longwood-seminars/video-archive/2017-longwood-seminars-video-archive

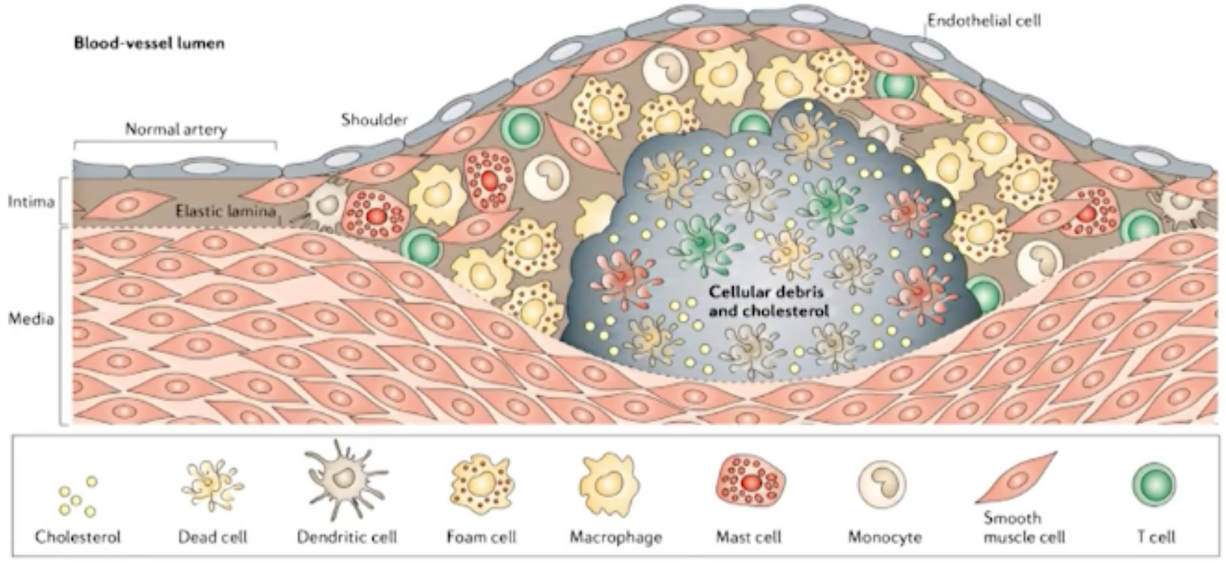
Inflammation & Cardiovascular Disease

Plaques contain many immune cells



Robbins, Hilgendorf, et al., *Nat Med* 2013.

Leukocytes in atherosclerosis

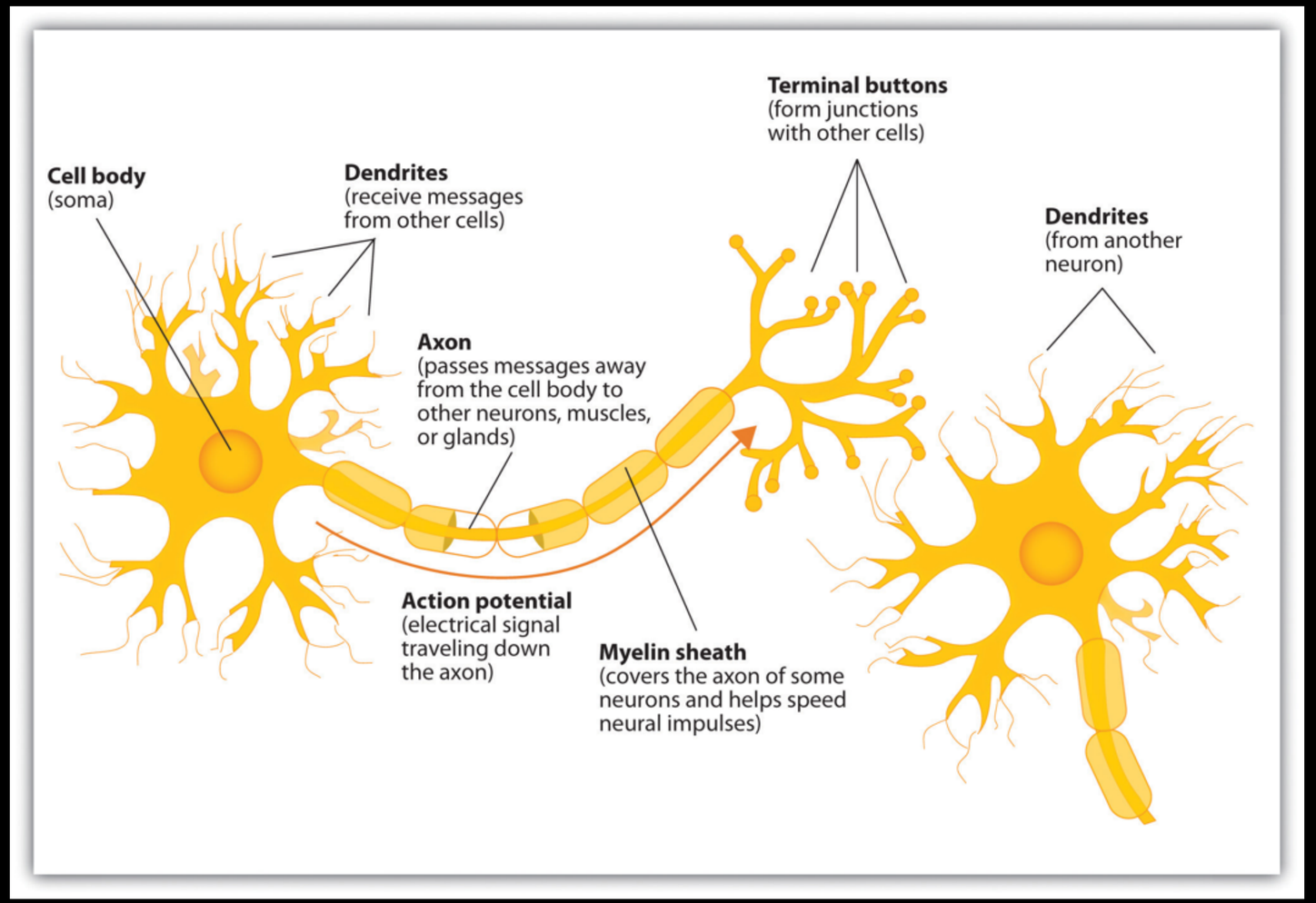


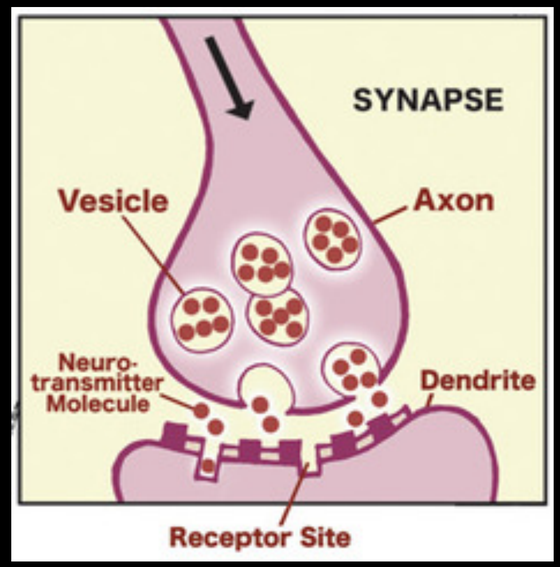
Hansson GK & Libby P. Nat. Rev. Immunol. 2006; 6:508-19.

https://hms.harvard.edu/news-events/longwood-seminars/video-archive/2017-longwood-seminars-video-archive

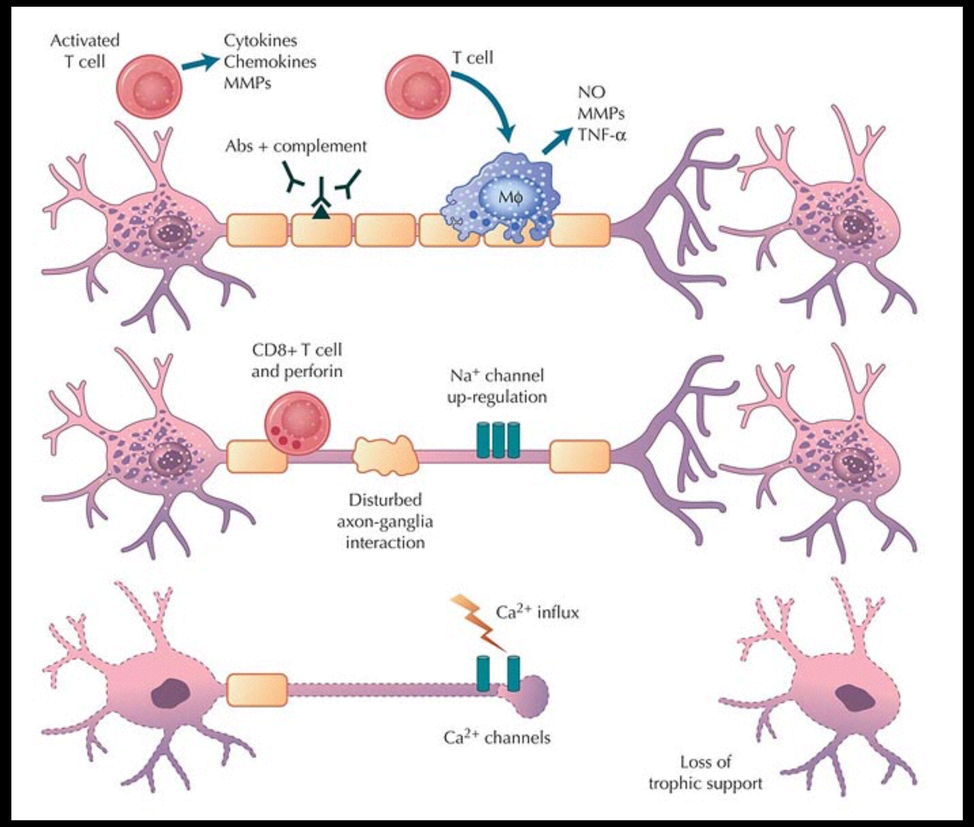
Basic Functional Unit - Nervous System

NEURON: the basic functional unit of the nervous system.





Inflammation & Neurologic Problems

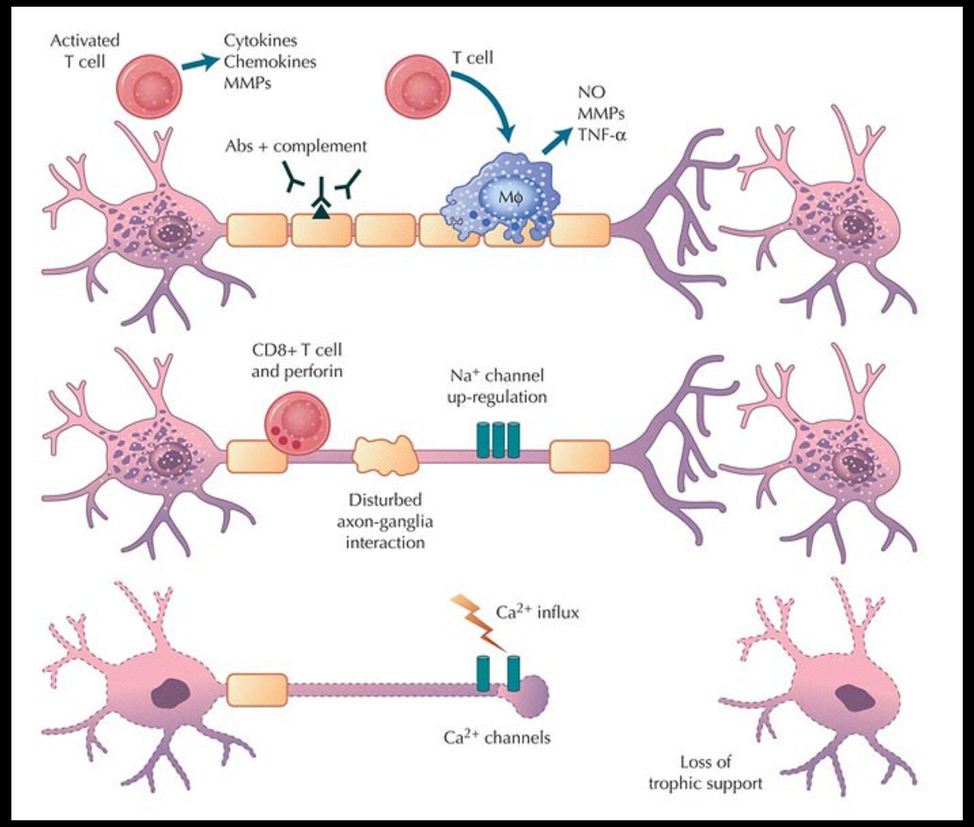


Cascade of events possibly underlying demyelination and axonal degeneration in multiple sclerosis: cont

- CD8+ cells are capable of attacking the axon and oligodendrocytes directly.
- The combination of toxic signals and the disturbed axon-glia interaction pave the way for axonal degeneration.
- The up-regulation of Ca2+ channels and the increased Ca2+ influx might perpetuate this process.
- High-frequency signaling of neurons results in axonal degeneration, especially upon exposure to nitric oxide.
- The loss of signaling activity and trophic support might contribute to axonal degeneration in connected neurons as well.
- Manifestation of the degenerative effects of chronic inflammation.

Current Neurology and Neuroscience Reports
Volume 3, Number 3: May 2003 • Demyelinating Disorders • pp. 246-255
Bernhard Hemmer, MD, Bernd Kieseier, MD, Sabine Cepok, and Hans-Peter Hartung, MD

Inflammation & Neurologic Problems



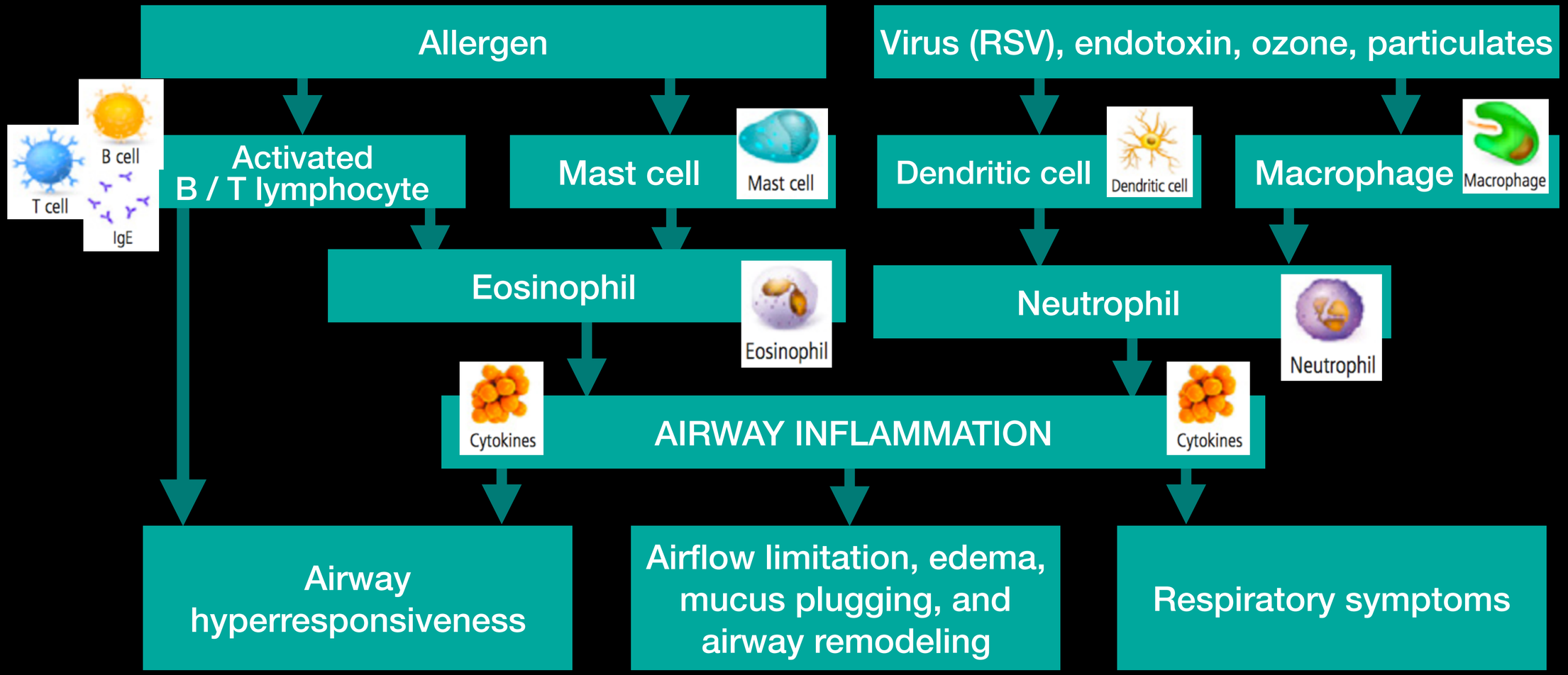
Cascade of events possibly underlying demyelination and axonal degeneration in multiple sclerosis:

- Within the central nervous system, activated T lymphocytes release inflammatory cytokines, chemokines, and matrix metalloproteinases (MMPs).
- Moreover, T cells activate microglia cells/macrophages to enhance phagocytic activity, the production of cytokines, and the release of toxic mediators such as nitric oxide (NO), propagating demyelination and axonal loss.
- Autoantibodies (Abs) crossing the blood-brain barrier or locally produced by B cells or mast cells contribute to this process.
- Autoantigens activate the complement cascade, resulting in the formation of the membrane-attack complex and subsequent lysis of the target structure.

Current Neurology and Neuroscience Reports
Volume 3, Number 3: May 2003 • Demyelinating Disorders • pp. 246-255
Bernhard Hemmer, MD, Bernd Kieseier, MD, Sabine Cepok, and Hans-Peter Hartung, MD

Inflammation & COPD

Postulated cellular mechanisms involved in airway inflammation



(Adapted from Douwes et al., 2002)

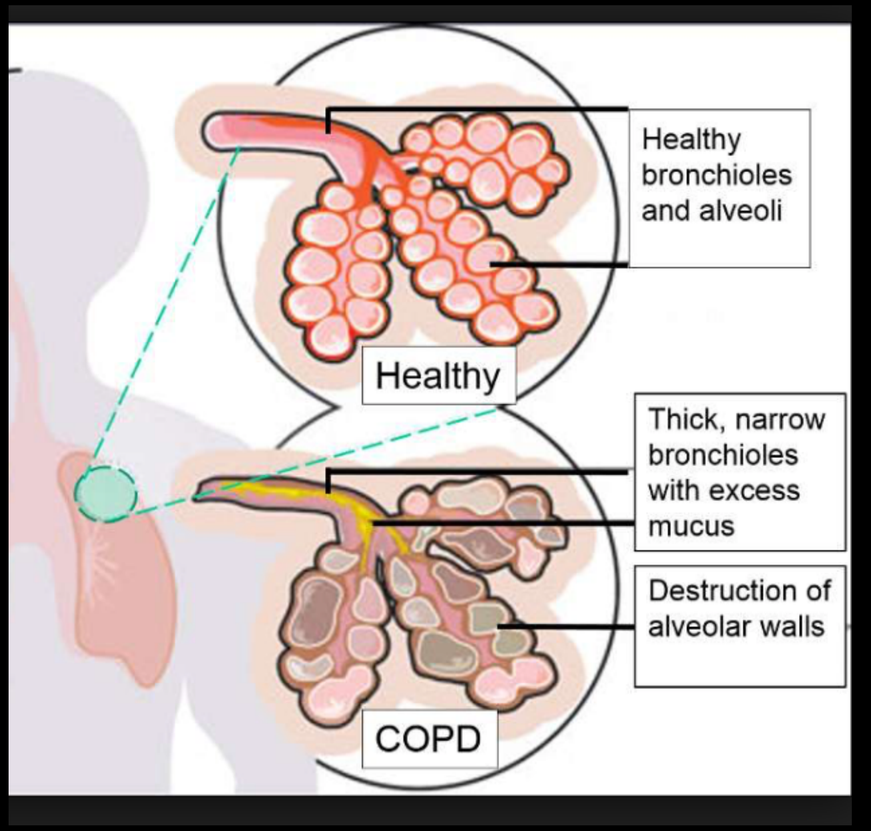
Inflammation & COPD

Factors driving decline in lung function

Smoking **+** → Muscle weakness; Respiratory infections; Oxidative Stress; **INFLAMMATION** ← **–** Physical activity

↓

Chronic Obstructive Pulmonary Disease manifestions

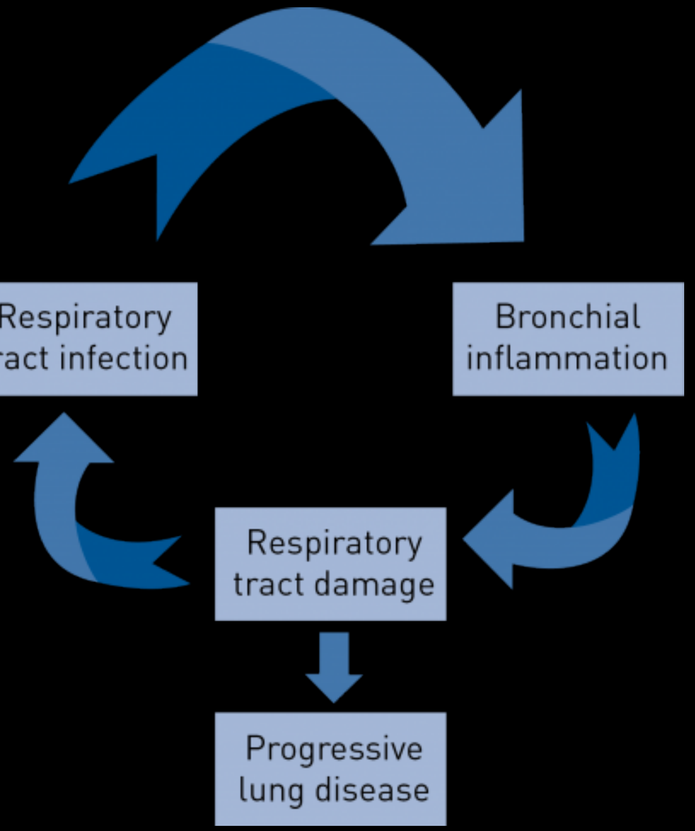


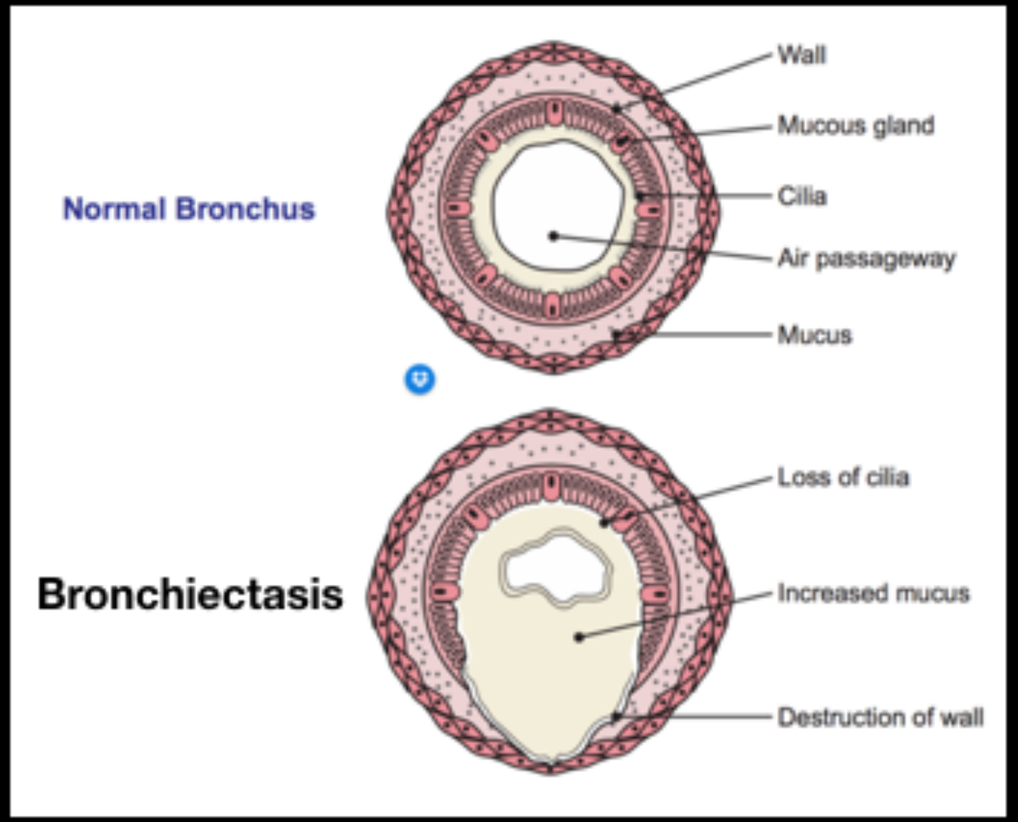
Does physical inactivity cause chronic obstructive pulmonary disease?
Nicholas S. Hopkinson, Michael I. Polkey. Clinical Science, Feb 09, 2010, 118 (9) 565-572;
DOI: 10.1042/CS20090458

Inflammation & COPD

The vicious cycle of infection and inflammation
leading to progressive lung disease in bronchiectasis.

1) Microbial insults
2) Defect in host defense

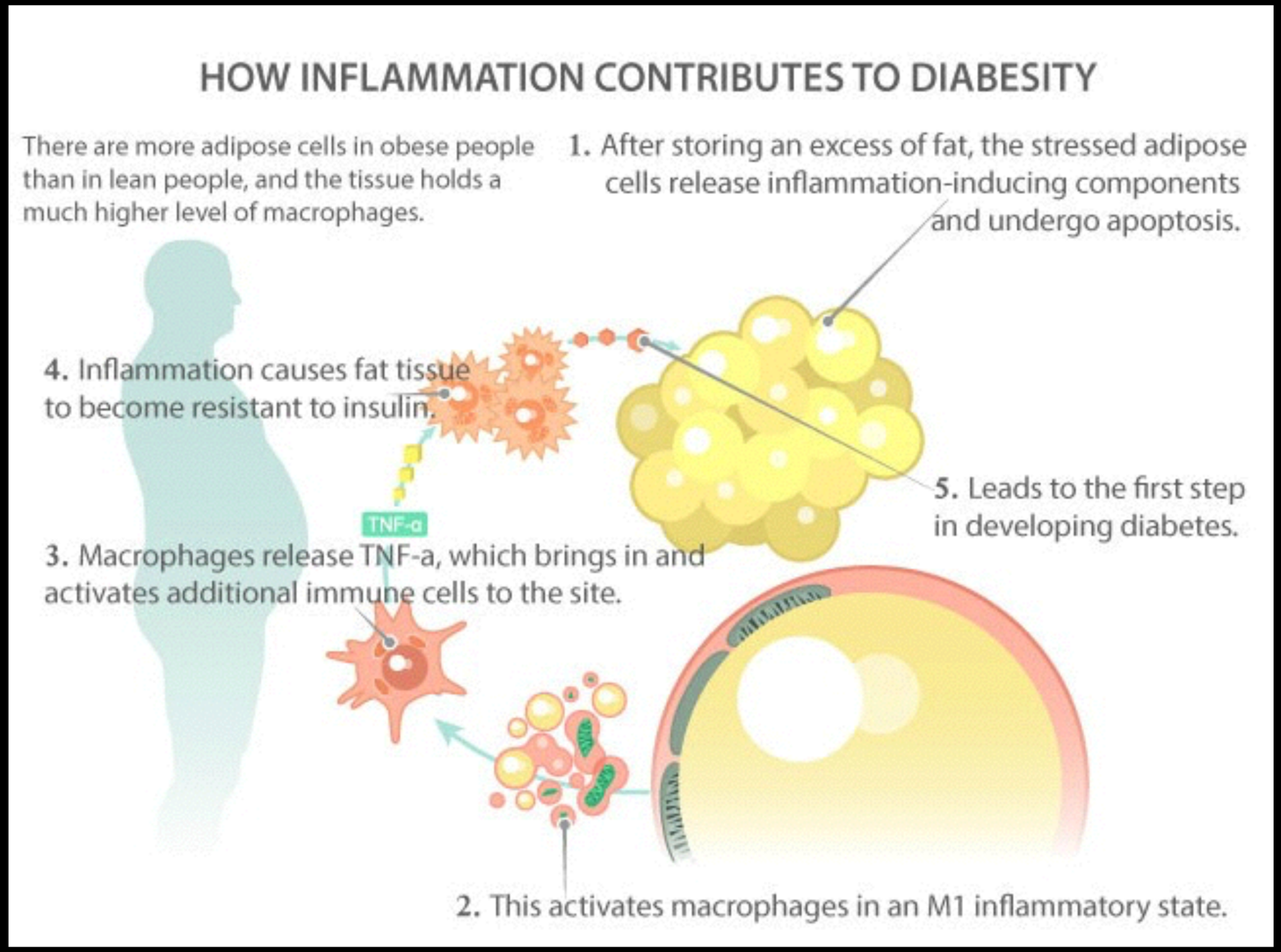




EUROPEAN LUNG *white book*

https://www.erswhitebook.org/chapters/bronchiectasis/

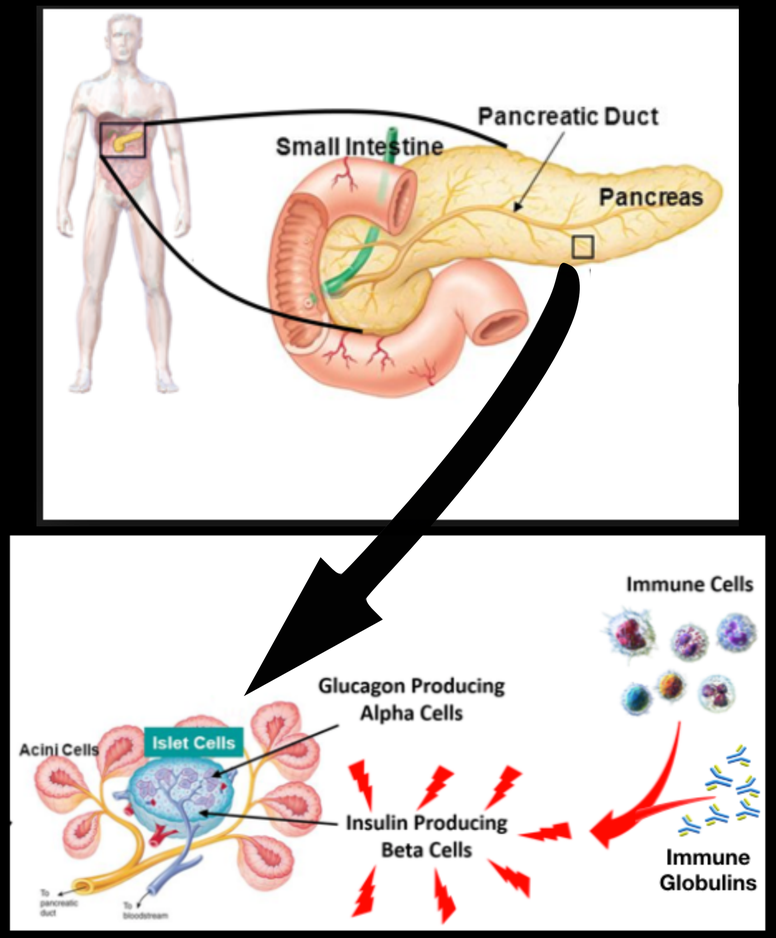
Inflammation & Diabesity



G.S. Hotamisligil, *et al.* Adipose expression of tumor necrosis factor-α: direct role in obesity-linked insulin resistance. *Science*, 259 (1993), pp. 87–91.
Jerrold M. Olefsky and Christopher K. Glass "Macrophages, Inflammation, and Insulin Resistance." *Annual Review of Physiology* Vol. 72: 219-246 March 2010

Inflammation & Diabetes Mellitus II

Type-1 Diabetes Initiation



https://www.andrewkoutnik.com/blog/2018/8/22/part-1-what-is-type-1-diabetes

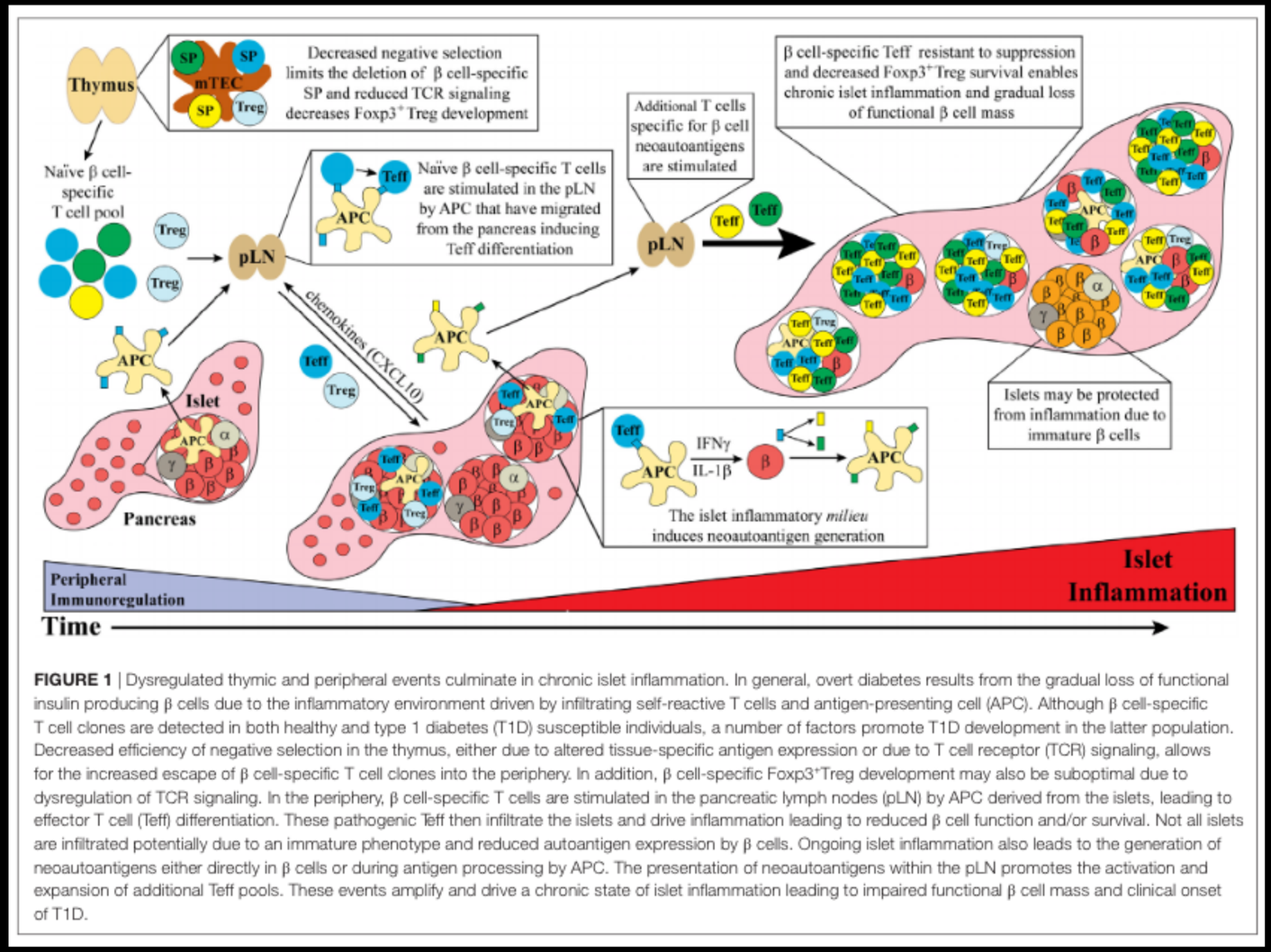
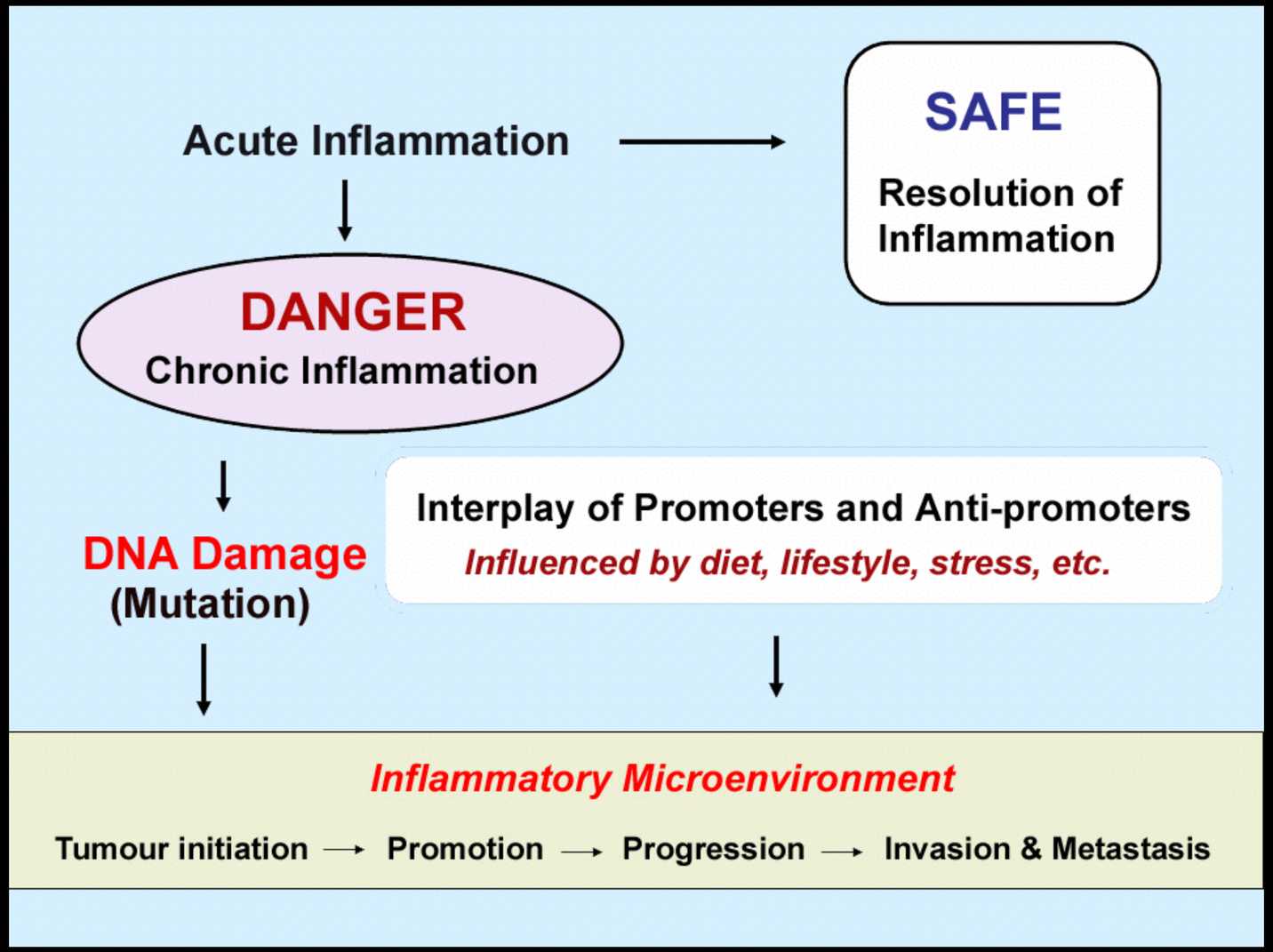


FIGURE 1 | Dysregulated thymic and peripheral events culminate in chronic islet inflammation. In general, overt diabetes results from the gradual loss of functional insulin producing β cells due to the inflammatory environment driven by infiltrating self-reactive T cells and antigen-presenting cell (APC). Although β cell-specific T cell clones are detected in both healthy and type 1 diabetes (T1D) susceptible individuals, a number of factors promote T1D development in the latter population. Decreased efficiency of negative selection in the thymus, either due to altered tissue-specific antigen expression or due to T cell receptor (TCR) signaling, allows for the increased escape of β cell-specific T cell clones into the periphery. In addition, β cell-specific Foxp3+Treg development may also be suboptimal due to dysregulation of TCR signaling. In the periphery, β cell-specific T cells are stimulated in the pancreatic lymph nodes (pLN) by APC derived from the islets, leading to effector T cell (Teff) differentiation. These pathogenic Teff then infiltrate the islets and drive inflammation leading to reduced β cell function and/or survival. Not all islets are infiltrated potentially due to an immature phenotype and reduced autoantigen expression by β cells. Ongoing islet inflammation also leads to the generation of neoautoantigens either directly in β cells or during antigen processing by APC. The presentation of neoautoantigens within the pLN promotes the activation and expansion of additional Teff pools. These events amplify and drive a chronic state of islet inflammation leading to impaired functional β cell mass and clinical onset of T1D.

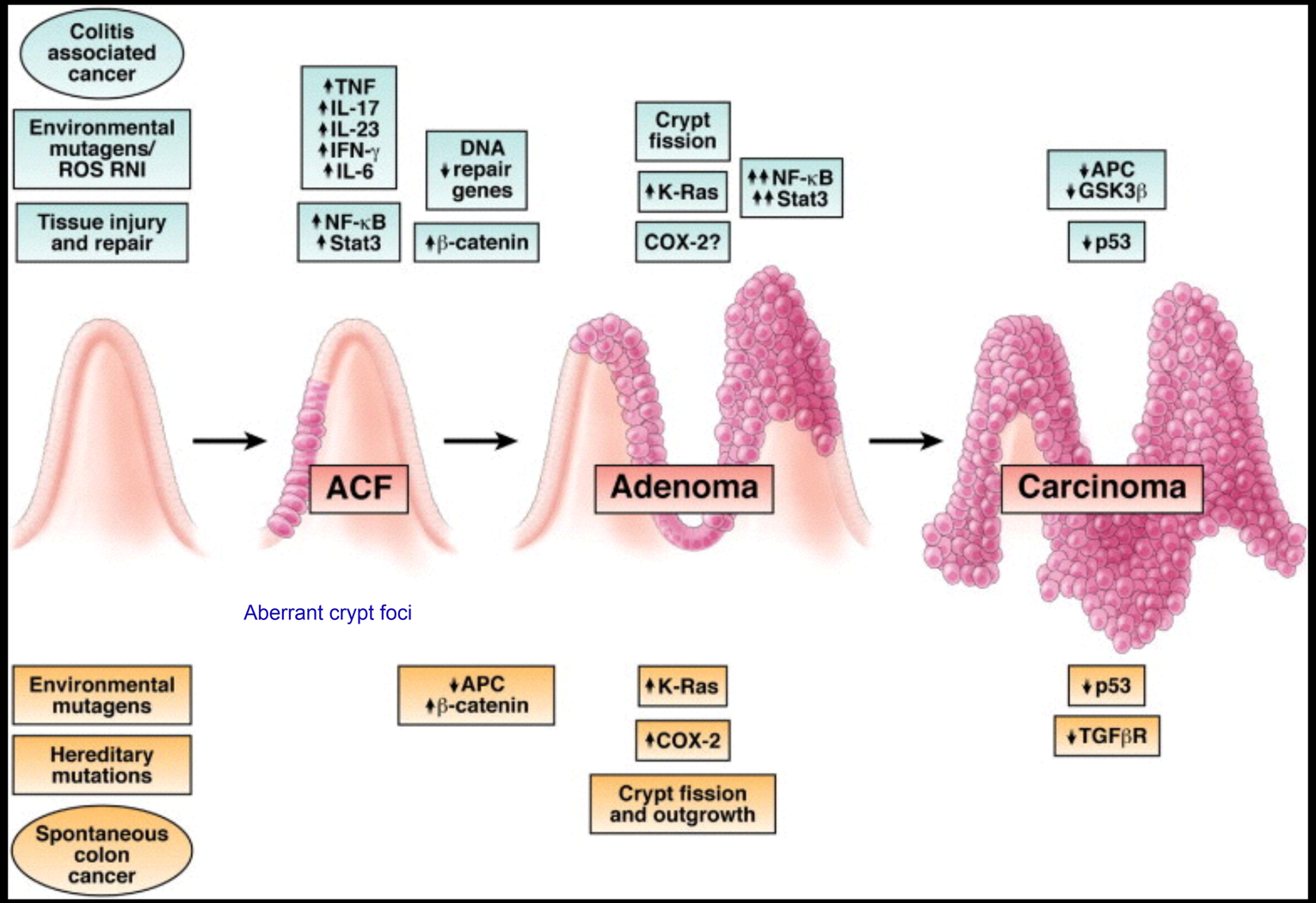
Clark M, Kroger CJ & Tisch RM (2017) Type 1 Diabetes: A Chronic Anti-Self-Inflammatory Response. Front. Immunol. 8:1898
doi: 10.33899/fimmu.2017.01898

Inflammation —> Cancer



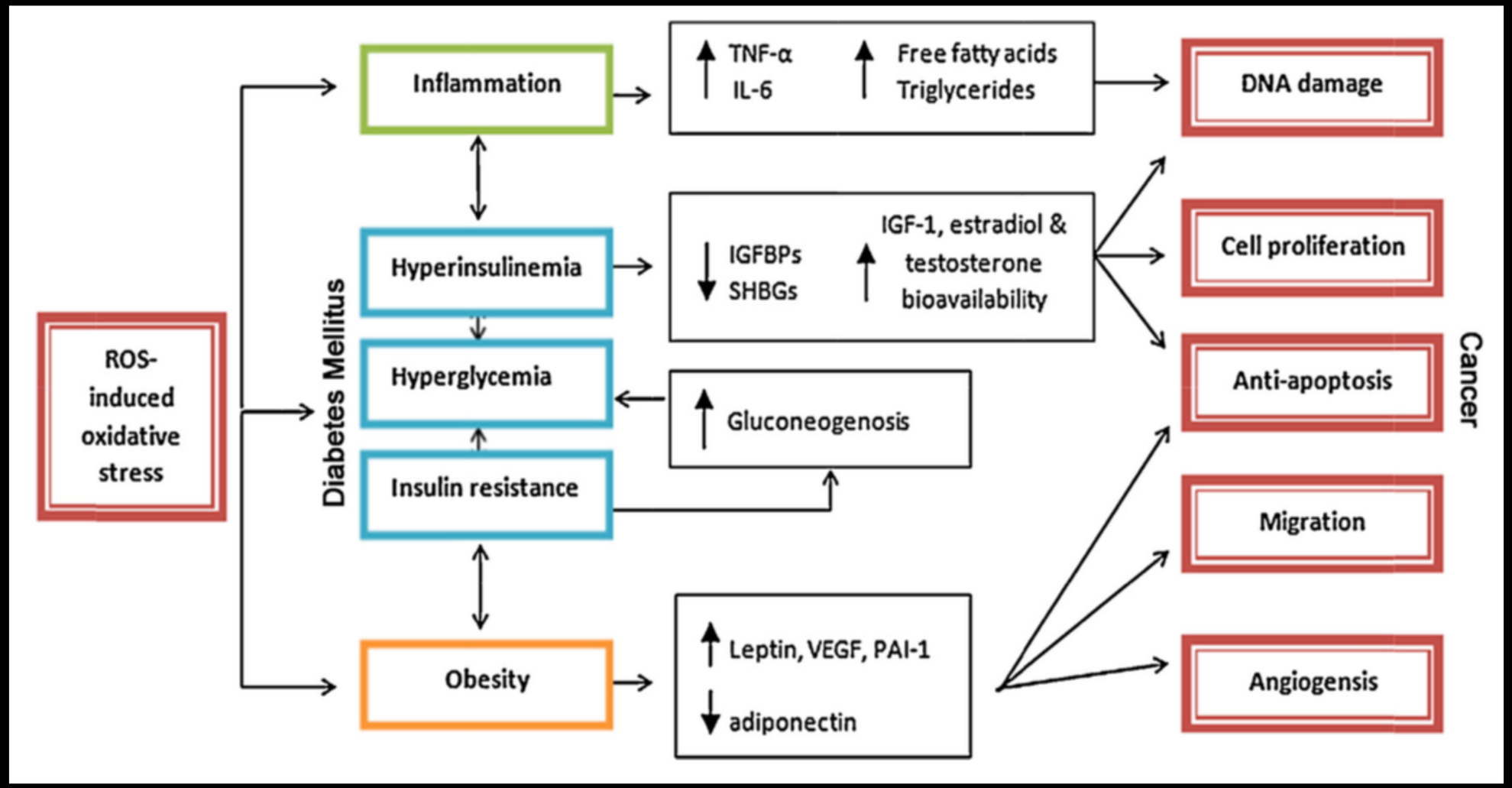
https://ejtcm.com/2011/03/19/inflammation-and-cancer/

Inflammation —> Cancer



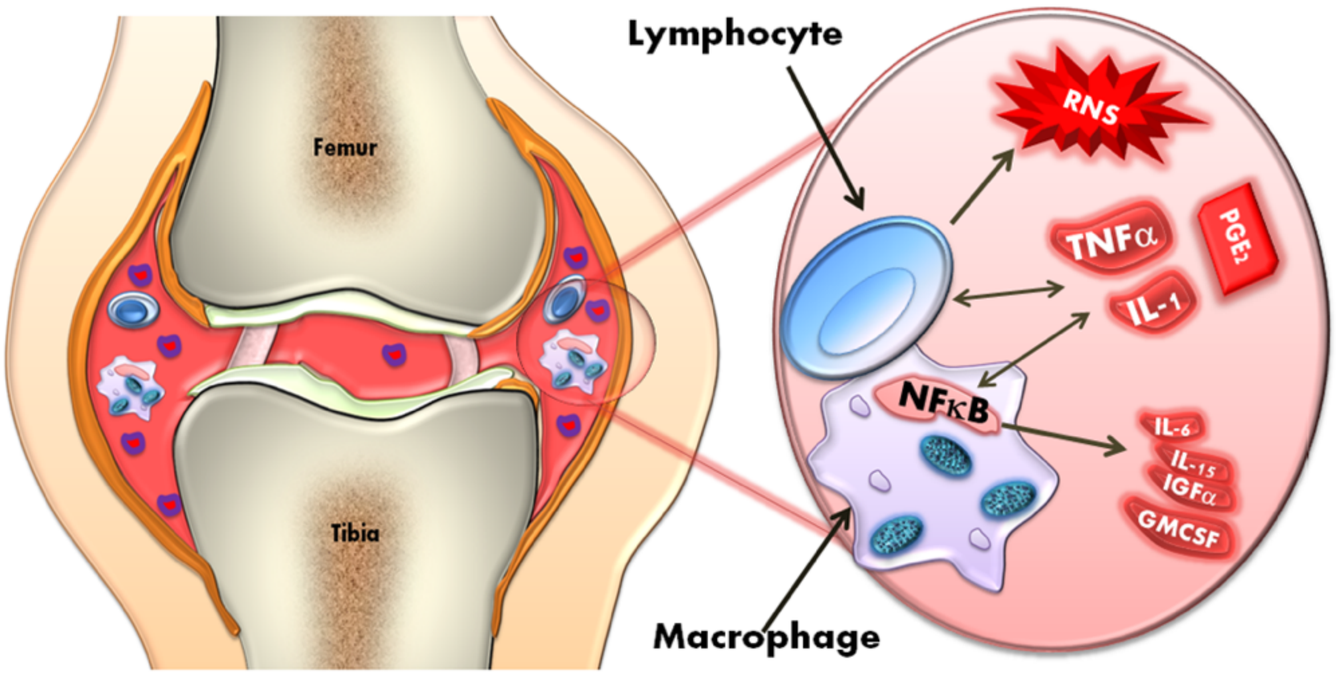
Inflammation and Colon Cancer. Terzic J.Greviennikov S, Karin e, Karin M, Gastroenterology, vol.138, issue 6, May 2010, pages 2101-2114

Inflammation, Cancer & Diabetes



O.I. Aruoma et al. / Mutation Research 768 (2014) 60–68

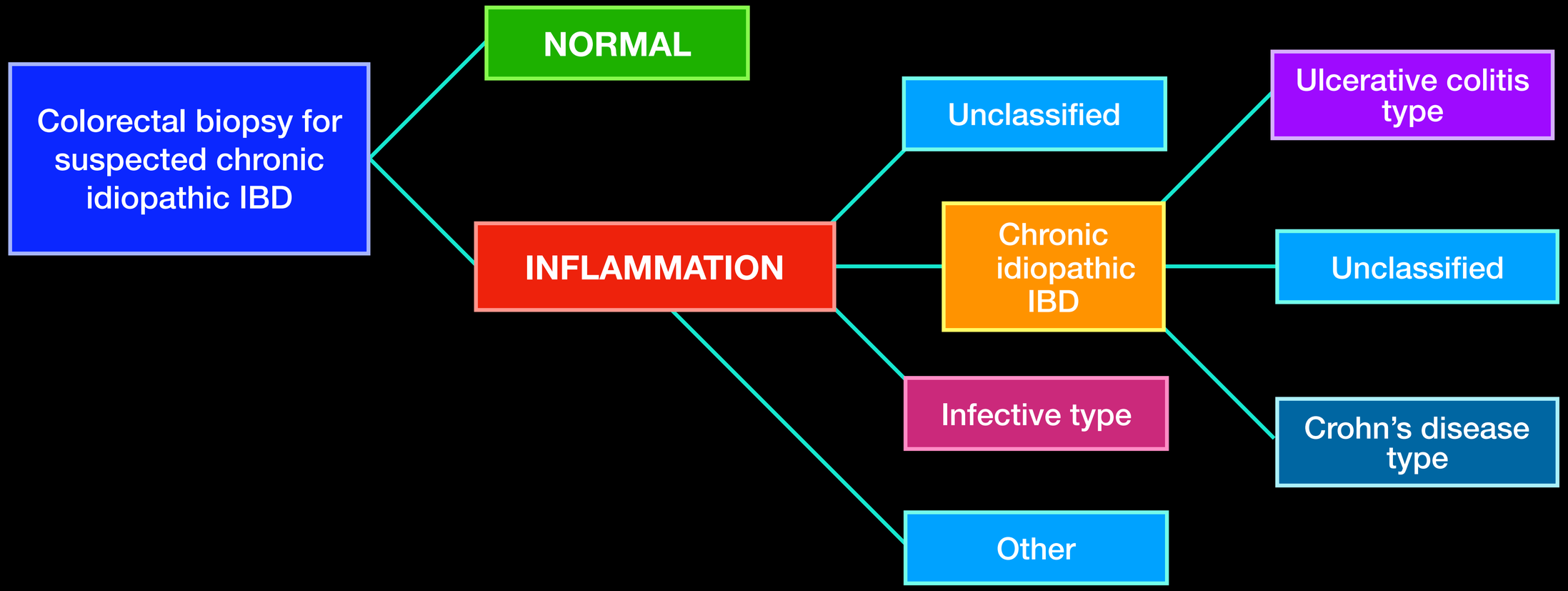
Inflammation & Arthritis



In Rheumatoid Arthritis joints, immune cells (lymphocytes, macrophages, neutrophils…etc.) produce inflammatory Cytokines, Reactive Oxygen / Nitrogen Species (ROS / RNS).

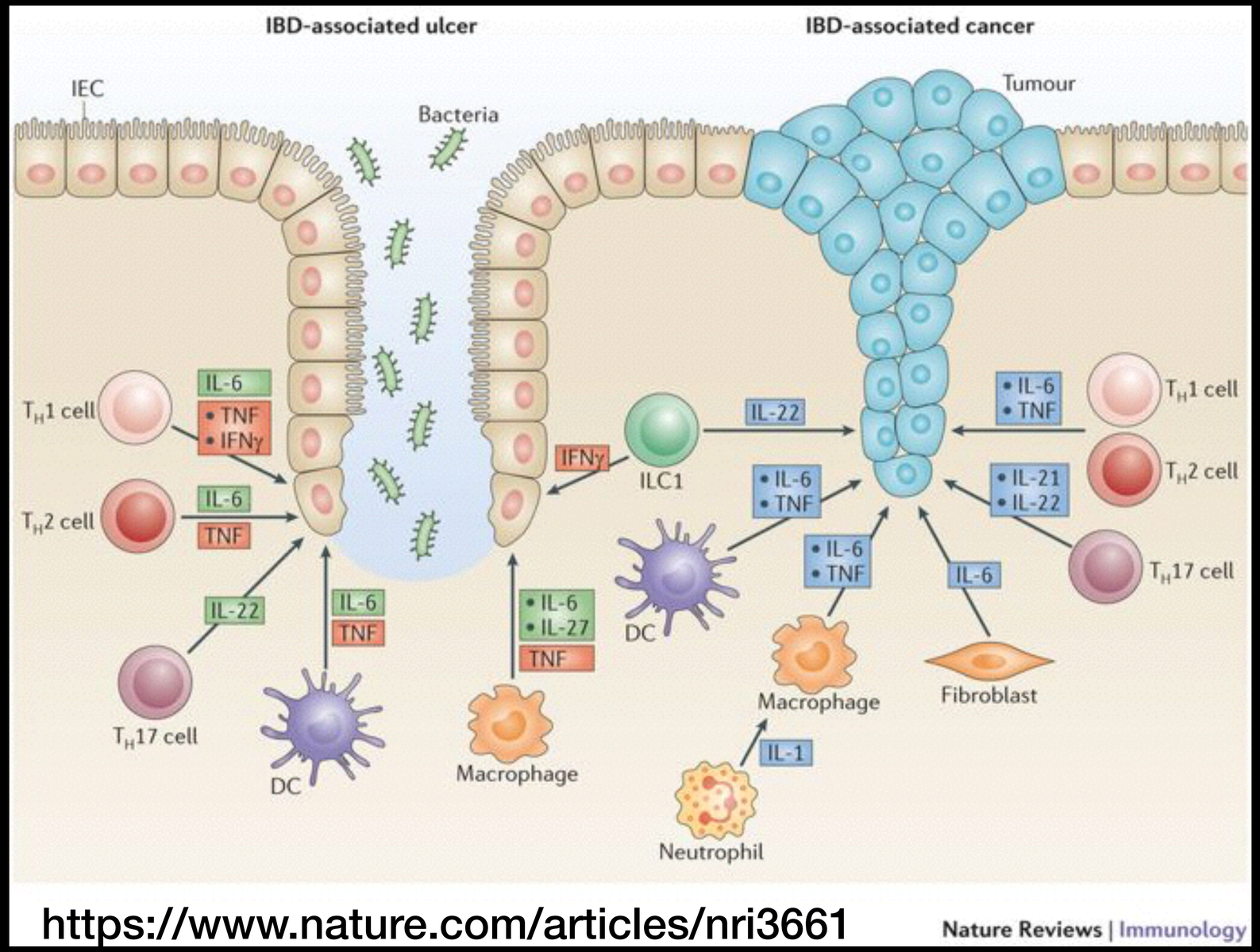
NUTRITIONREMARKS
BASED ON SCIENTIFIC EVIDENCE

Inflammation & Inflammatory Bowel Disease



The BSG Inflammatory Bowel Disease Pathology Initiative. Jenkins et al, 1997

Inflammation & Inflammatory Bowel Disease



https://www.nature.com/articles/nri3661

Why the Epidemic of Chronic Diseases

**

Nutr Metab (Lond). 2012 Apr 17;9(1):32. doi: 10.1186/1743-7075-9-32.

Chronic inflammatory diseases are stimulated by current lifestyle: how diet, stress levels and medication prevent our body from recovering.

Bosma-den Boer MM[1], van Wetten ML, Pruimboom L.

- In recent decades there has been a tremendous acceleration in innovations which have changed our lives completely,
- > 75% of humans do not meet the minimum requirement of the estimated necessary daily physical activity,
- 72% of modern food types is new in human evolution,
- Psycho-emotional stress has increased, and
- Man is exposed to an overwhelming amount of information on a daily basis.

Why the Epidemic of Chronic Diseases

Systems Biology - new way of understanding disease (only of late)

- This dictates that chronic disease is complex and never involves just one organ or organ system. It involves underlying physiologic systems affecting the whole organism.
- With use of a systematic examination of an individual's physiologic imbalances that include mind, body, and spirit, a more robust identification of metabolic priorities can be achieved.
    - The registered dietitian nutritionist (RDN), as a member of the health care team, has a larger role to improve the nutritional status of each individual with dietary and lifestyle modifications as a foundational component of addressing chronic disease.

Why the Epidemic of Chronic Diseases

"A practice that is laying the foundation of a vast amount of disease and of even more serious evils is the free use of poisonous drugs.

"Our artificial civilization is encouraging evils destructive of sound principles." MH 126

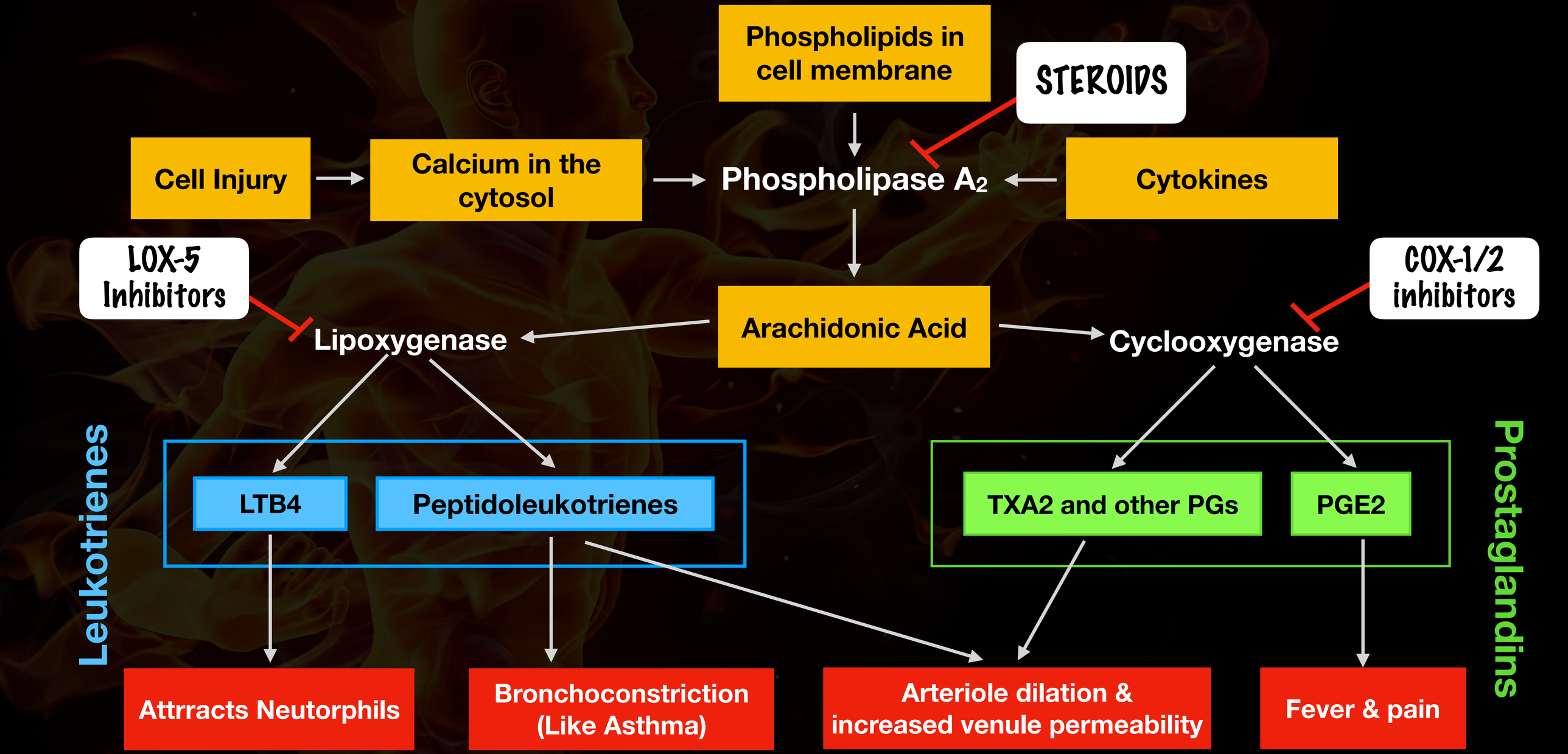
Inflammation: How to Diagnose It

- **INFLAMMATORY MARKERS:**
  1. CRP-hs in the plasma
  2. Erythrocyte Sedimentation Rate
  3. Interleukin-6
  4. TNF-α
- Diseases well characterized by these markers include heart disease, diabetes, autoimmune disease, and possibly cancer and Alzheimer's disease.
- Prolonged inflammation in-utero—> sets the fetus up for possible chronic diseases in the future.

Inflammation- How to “Zap It” <— Rx vs Herbs

- **Allopathic Medications:**
  - **Corticosteroids-** inhibits the change of arachidonic acid into leukotrienes and prostaglandins
  - **Non-Steroidal Anti-Inflammatory Drugs (NSAID)-** inhibit LOX and COX enzymes- eg, aspirin, ibuprofen, naproxen, diclofenac, indomethacin
    - LOX-5 inhibitor
    - COX-1/2 inhibitors
  - **NOSH*-NSAIDS** (added Nitric oxide / Hydrogen sulfide)

Physiology Behind Initial Inflammation cont.



Inflammation- How to “Zap It” - Rx vs Herbs

- **Allopathic Medications:** cont.
  - **Immunomodulators-** slows the production of the immune cells, thus reducing the cytokines- e.g., methotrexate
  - **Aminosalicylates-** inhibits the influx of WBC into the bowel wall for IBD- e.g., balsalazide, mesalamine, sulfasalazine
  - **Disease-modifying antirheumatic drugs (DMARDs)**
  - **Biologic drugs-** reduce production of cytokines- TNF inhibitor (Humira), tolizumab (Cimzia) & interleukin inhibitors like anakinra (Kineret)

Inflammation- How to “Zap It” - Rx vs Herbs

Immunemodulators

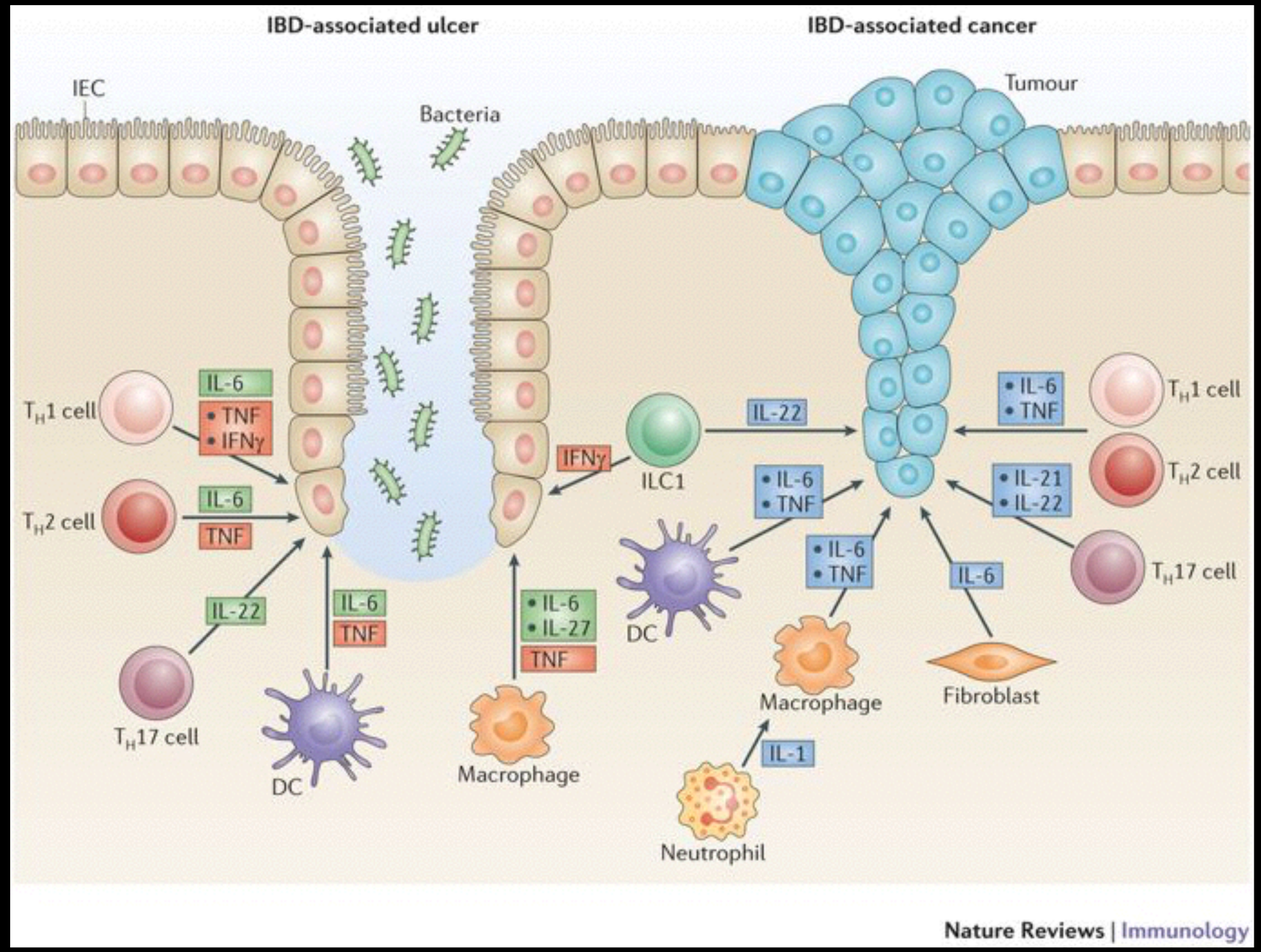
- They inhibit the production of inflammatory cells

Aminosalicylates

- They inhibit the influx of inflammatory cells into the affected areas

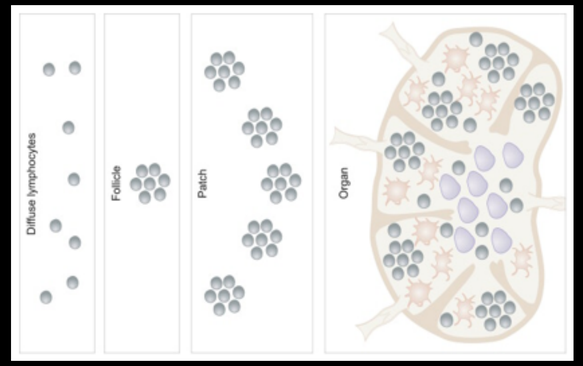
Biologic drugs

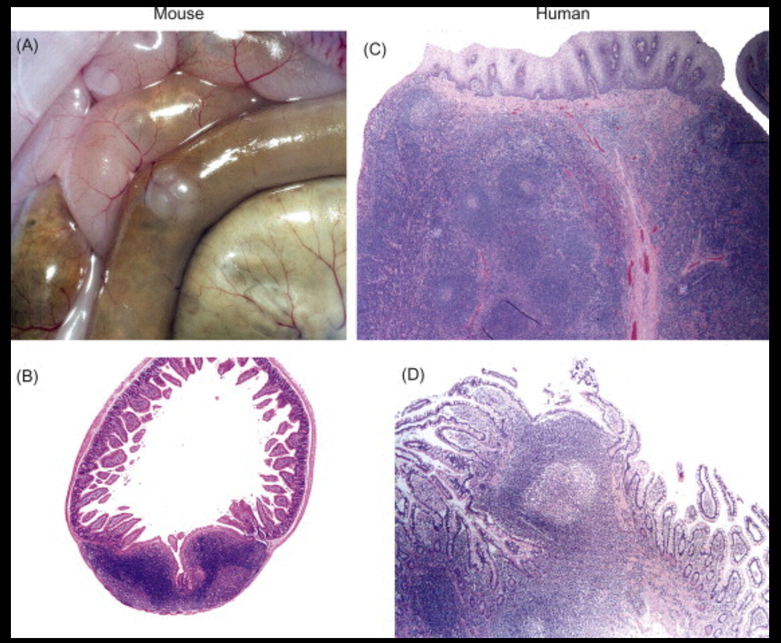
- They inhibit the effect of TNF



Inflammation- How to “Zap It” <— Gut Care

- **Gut ecology and the microbiome:**
  - The gastrointestinal tract has many functions in the health of an individual, and one of them is in immune integrity.
  - This is because the largest immune organ is located within the gastrointestinal tract as gut-associated lymphoid tissue (GALT), both with innate and acquired immune systems as well as about 3 pounds of symbiotic microbial organisms.
  - The condition of the gut lymphoid tissue and the microbial ecology has a large influence on the body’s inflammatory state.





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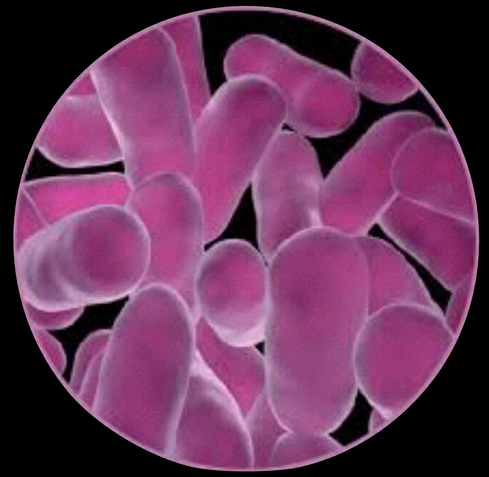
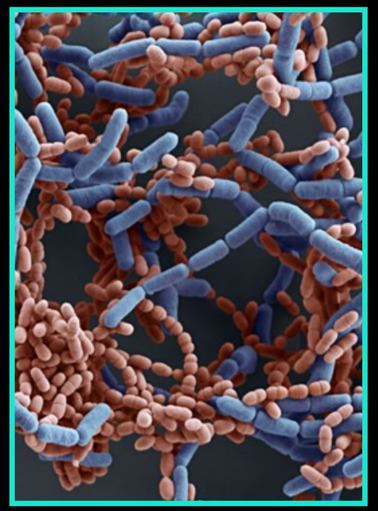
https://www.sciencedirect.com/topics/immunology-and-microbiology/lymphoid-tissue

Inflammation- How to “Zap It” <— Gut Care

- **Gut ecology and the microbiome:**
  - The inverse relationship of gut barrier integrity and ecology with organ specific or systemic inflammation is well documented.
  - Medical nutrition therapy recommendations for increasing fermented foods, lowering intake of processed foods, avoiding gastrointestinal irritating foods and any known antigens for an individual, are basic to improving the microbial ecology.
  - Therapeutic use of functional foods, pre- and probiotics, and supplements can sometimes be indicated to restore optimum gut function and reduce inflammation.





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Inflammation- How to “Zap It” - Rx vs Herbs

- **HERBAL SUPPLEMENTS:**
  - **Boswellia-** (aka Indian Frankinsence) has 4 acids that have **anti-inflammatory** properties. These acids inhibit 5-lipoxygenase (5-LO), an enzyme that produces leukotriene
  - **Turmeric-** is a non-specificanti-inflammatory agent inhibiting both lipoxygenase and cyclooxygenase-1/2
  - **Ashitaba-** (*Angelica keiskei*) stimulates NGF
  - **Bromelain-** (from pineapple) selectively inhibits the biosynthesis of proinflammatory prostaglandins

Indian J Pharm Sci. 2011 May-Jun; 73(3): 255–261. doi: 10.4103/0250-474X.93507
https://www.ncbi.nlm.nih.gov/pubmed/17569207
http://ashitabaplant.blogspot.com/2011/06/ashitaba-stimulates-nerve-growth-factor.html

Inflammation- How to “Zap It” <— Lifestyle

- **HEALTHY LIFESTYLE HABITS**
  - Exercise regularly
  - Manage body weight
  - No smoking
  - Get enough good sleep
  - Stress management
  - Healthy relationships

https://www.nejm.org/doi/full/10.1056/NEJMra003200

Inflammation- How to “Zap It” <— Lifestyle

- EATING WISELY
- **Food**
  - **medically**, any substance that the body can take in and assimilate that will enable it to stay alive and to grow; the carrier of nourishment;
  - **socially**, a more limited number of such substances defined as acceptable by each culture.

Ingredients: Enriched Corn Meal (Corn Meal, Ferrous Sulfate, Niacin, Thiamin Mononitrate, Riboflavin, and Folic Acid), Vegetable Oil (Corn, Canola, Soybean, and/or Sunflower Oil), Cheese Seasoning (Whey, and less than 2% of the following: Cheddar Cheese [Milk, Cheese Cultures, Salt, Enzymes]. Partially Hydrogenated Soybean Oil, Canola Oil, Maltodextrin (Made from Corn], Sour Cream [Cultured Cream, Skim Milk] Salt, Whey Protein Concentrate, MSG, Natural and Artificial Flavors, Lactic Acid, Citric Acid, Artificial Color [Including Yellow 6]), and salt.

Inflammation- How to “Zap It” <— Lifestyle

- EATING WISELY
- Multiple iterations of an anti-inflammatory diet exist:
  - DASH (Dietary Approaches to Stop Hypertension),
  - Mediterranean diet,
  - MIND (Mediterranean- DASH Intervention for Neurodegenerative Delay),
  - vegetarian (of all sorts),
  - food allergy elimination,
  - calorie restriction, and
  - low histamine.
- In most cases, overall dietary and lifestyle habits are more important to consider rather than any single change.

Inflammation- How to “Zap It” <— Lifestyle

- RECOMMENDED Anti-Inflammatory Food
  - Consume an abundance of fruits, vegetables, herbs, and spices.
  - Eat a low glycemic diet- take note about glycemic load
  - Have nuts and seeds
  - Adjust quality and quantity of fats and oils
  - Get adequate sources of probiotics
  - Consider food allergies or sensitivity elimination
  - Avoid chemicals- from food and containers

The Anti-Inflammatorydiet p. 99

Inflammation- How to "Zap It" <— Lifestyle

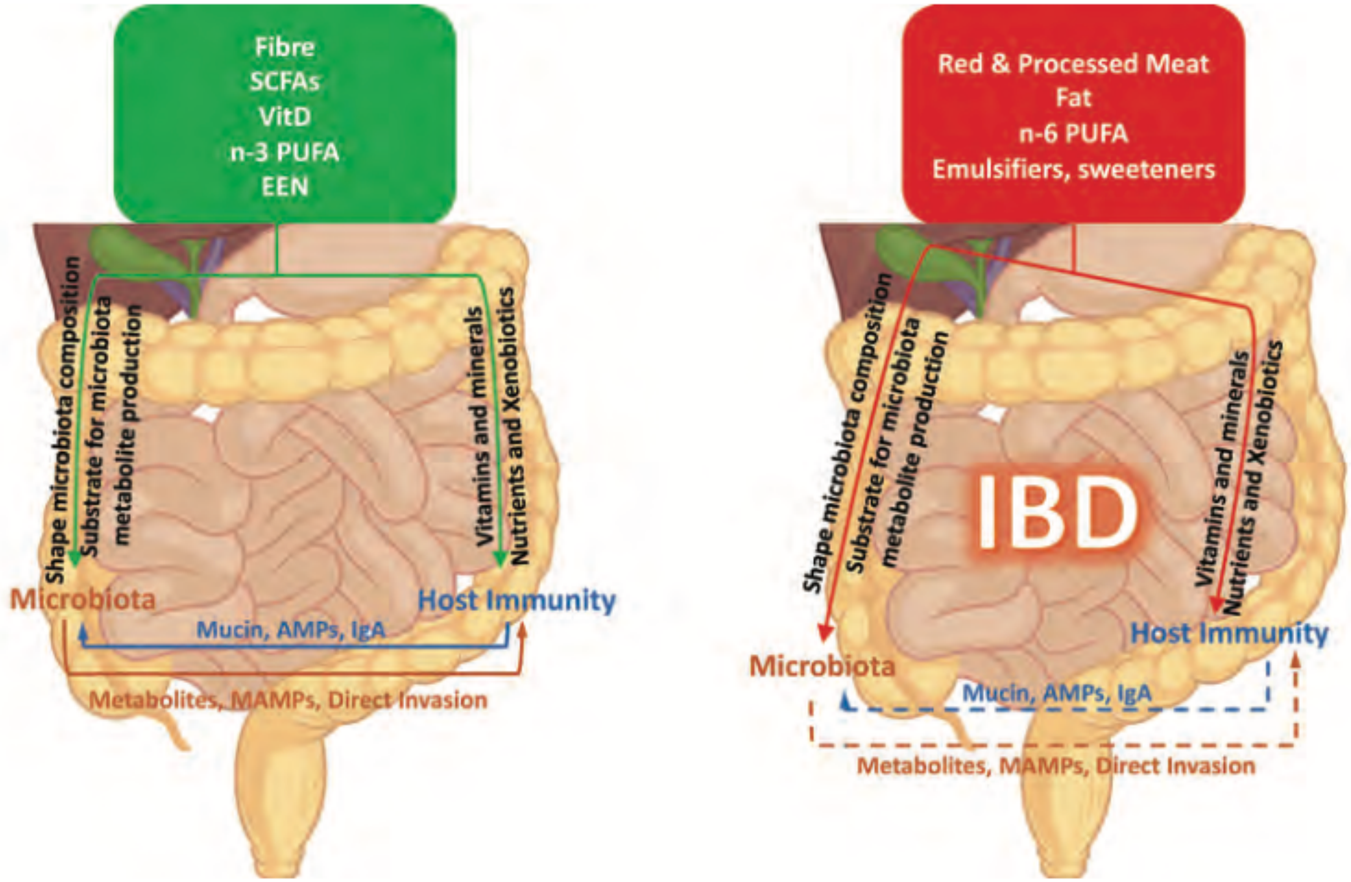

Figure 1. Diet regulation of microbiota and host immune responses in health and disease. Image adapted from "Lee D, Albenberg L, Compher C et al. Diet in the pathogenesis and treatment of inflammatory bowel diseases. Gastroenterology 2015, **148**(6):1087-106"

Inflammation- How to “Zap It” <— Lifestyle

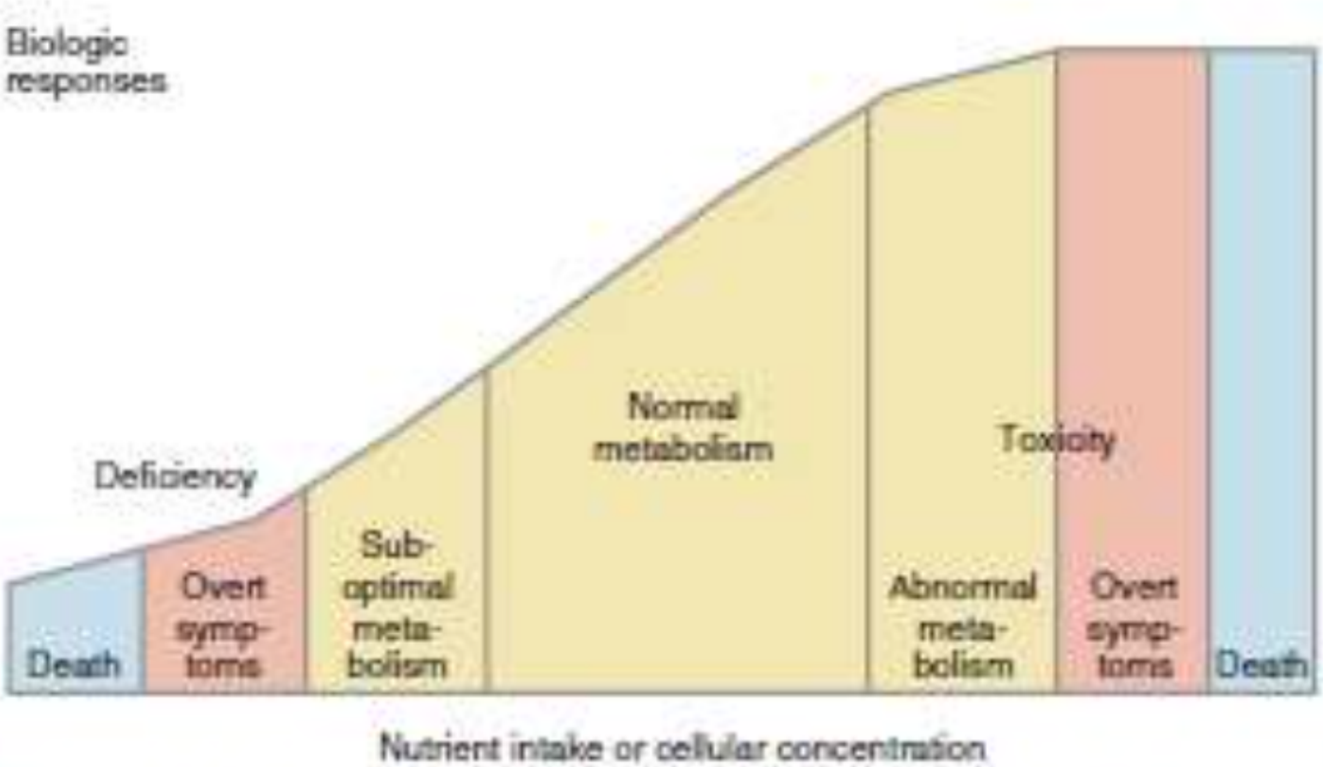

FIGURE 7-2 The size of a nutrient pool can vary continuously from frankly deficient, to adequate, to toxic.

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Inflammation- How to “Zap It” <— Lifestyle

- UNWAVERING SELF-CONTROL

Proverbs 23:7
“For as he thinkers in his heart, so is he…”

1 Corinthians 9:23
“And every man that striveth for the mastery is temperate in all things…”

Inflammation- How to “Zap It” <— Lifestyle

- HEALTHY RELATIONSHIPS

✓ Within the family

✓ Within the community

Inflammation- How to “Zap It” <— SUMMARY

- **Pro-inflammatory Influences**
  - Air pollution
  - Chronic stress
  - Environmental contaminants
  - Inactive lifestyle
  - Obesity
  - Processed food / Saturated fats
  - Sugar, trans-fat
  - Sleep deprivation
  - Smoking
  - Irregular routine

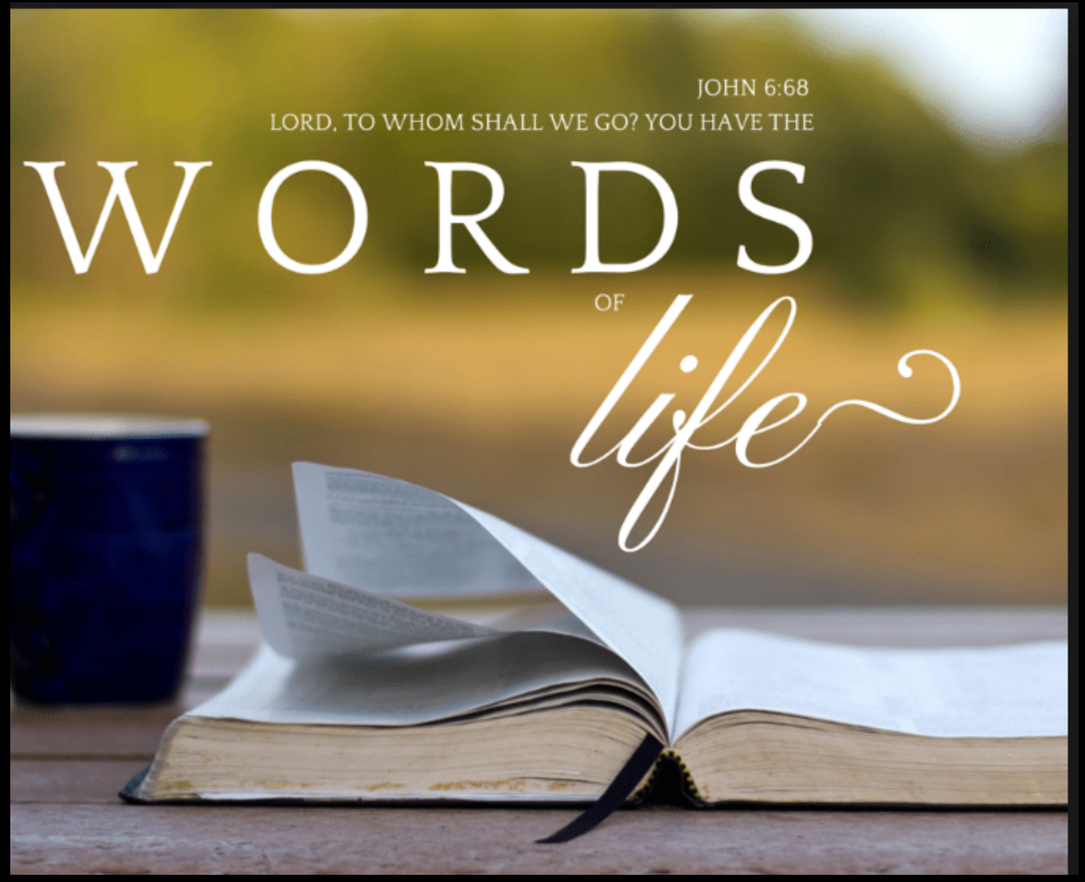
- **Anti-inflammatory Influences**
  - Eating to live (not live to eat)!
    - Fruits, vegetables beans and seeds
    - Whole vs refined grains (lectins/gluten)
    - Certain herbs, spices, tea and cocoa
    - Dietary fiber
    - Fruits vegetables and seeds
    - Mono/polyunsaturated vs saturated fats
      - Olive / coconut oil
      - Fish oils: Omega-3s vs omega-6
    - Healthy energy intake vs output
  - Physical activity
  - Steady, doable routine
  - Taking control of life, and

Inflammation- How to “Zap It” <— Lifestyle

- **TRUST in the DIVINE WORD**

3 John 2
Beloved friend, I pray that you are prospering in every way and that you continually enjoy good health, just as your soul is prospering. (TPT)

Jeremiah 29:11
For I have known the thoughts that I am thinking towards you -- an affirmation of Jehovah; thoughts of peace, and not of evil, to give to you posterity and hope. (YLT)



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May Your Immune Systems Be Blessed !