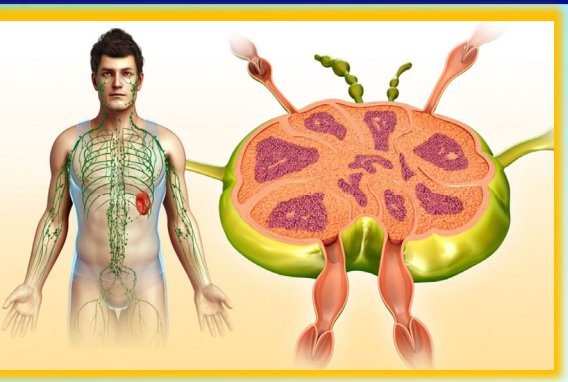
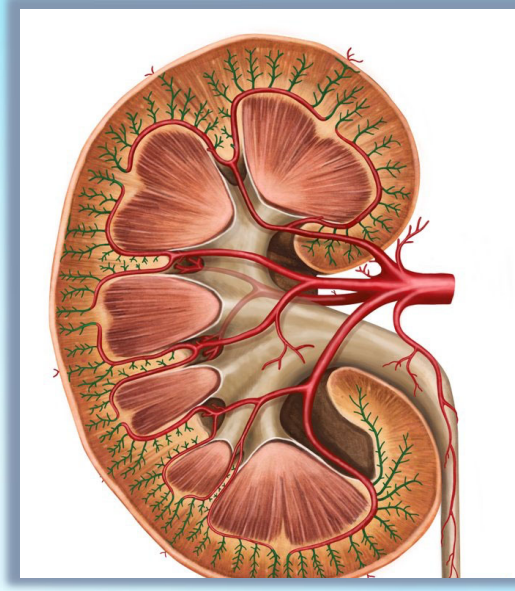
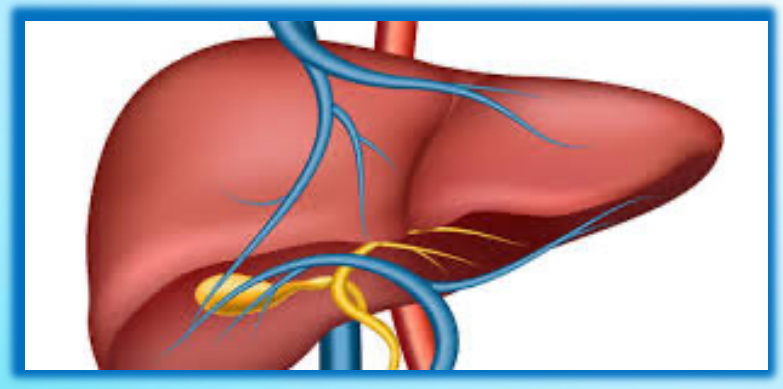




Liver – Lymph – Kidney - Axis of Detoxification

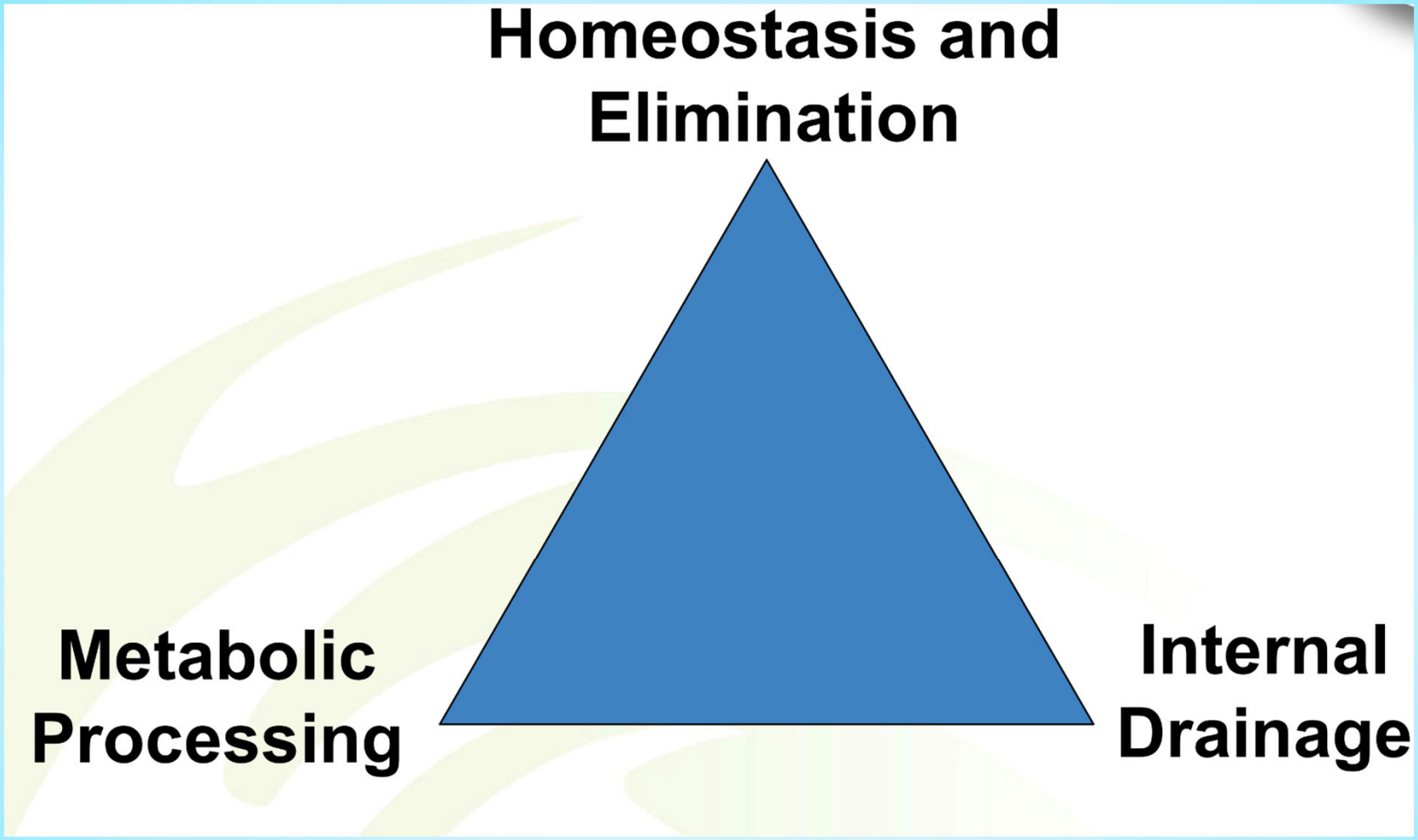


James LaValle, RPh, CCN, DHM, DHPh, N.D. (trad)
Founder and President, Metabolic Code Enterprises
Clinical Director Pro Football Hall of Fame
Performance Health

This material is provided for educational and informational purposes only to licensed health care professionals. This information is obtained from sources believed to be reliable, but its accuracy cannot be guaranteed. Herbs and other natural substances are very powerful and can occasionally cause dangerous allergic reactions in a small percentage of the population. Licensed health care professionals should rely on sound professional judgment when recommending herbs and natural medicines to specific individuals. Individual use of herbs and natural medicines should be supervised by an appropriate health care professional. The use of any specific product should always be in accordance with the manufacturer's directions.

Liver – Lymph – Kidney Axis

- Detoxification and Elimination
- REDOX potential and enzymatic activity
- Metabolic Processing and Removal
- NORMAL: Smooth flow of substrates and emotions
- IMBALANCED: Metaflammation, Stagnation, Retention


Homeostasis and Elimination
Metabolic Processing
Internal Drainage

What is Detoxification?

Definition

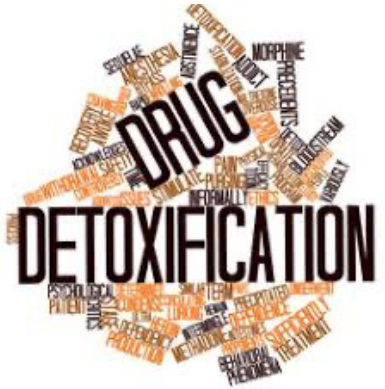
- Biochemical processes by which non water-soluble compounds are transformed into water soluble compounds that are then excreted by the body through urine, sweat, or stool

- Benefit: Protects body from adverse effects of external and internal toxins

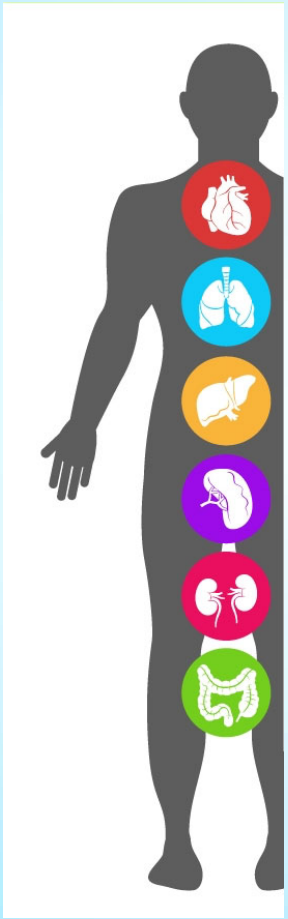
Who Needs to Detoxify ?

- The body should do it every day
- Take meds?
- Slow detoxification system + too many exposures over time= system overload
- Shifts the balance of intake and elimination out of kilter
- Everyone can benefit from detoxification
- Overflow or rain barrel effect leads to loss of ***metabolic reserve***

What detox isn't...



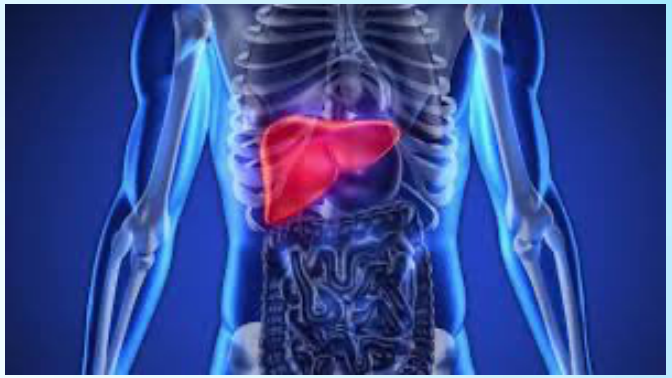
Organs of Detoxification



- Liver
- Lymphatic system
- Kidney
- Gallbladder
- Lungs
- Skin

Detoxification Imbalances

- Fatigue
- Allergies/intolerances
- Sluggish metabolism
- Weight gain easily
- Intolerance to fats
- Puffy – excess fluid
- Body odor, bad breath, metallic taste
- Profuse sweating even in cool weather



Toxins

- Chemicals that present an unreasonable risk of injury to health = Xenobiotics
- Each toxic substance has a defined toxic concentration or toxic dose
- Synergy between toxins, lowers threshold of harm
- Elimination of toxins shows great individual variability
- Toxins may cause immune and nervous system abnormalities even below the defined toxic dose
- Exposures are additive. Many are synergistic.
- Most toxins are fat soluble.
- Fat soluble toxins accumulate in fatty tissues, in particular the nerve sheath (myelin), brain, and liver.

How People Become Toxic

- Gender
- Genetics
  - Blood Type
  - HLA- Type
  - Family History of Autoimmunity
  - Single Nucleotide Polymorphisms (SNP) causing impaired detoxification (COMT, MTHFr, TCII, MTR)
- Heavy Metal and Toxic Burden
  - Mom (amalgams, fish consumption, vaccines, environmental toxics, occupation, oral contraceptives)
  - Person (immunizations, environmental toxins, antibiotics, immune issues, gastrointestinal permeability, drugs)
- Infectious Agents
  - Virus (Measles, CMV…)
  - Bacteria (Streptococcus, Clostridia…)
  - Fungal (Candida)

Environmental Pollutants are Making Headlines

- NHANES data in Children 2011-2012
- "We found associations between markers of phthalate exposure and testosterone levels among multiple age groups and in both sexes, including children — 6- to 12-year-old boys and girls, and girls ages 12 to 20," lead author John D. Meeker, ScD, CIH,

Urinary Phthalate Metabolites Are Associated With Decreased Serum Testosterone in Men, Women, and Children From NHANES 2011–2012 http://dx.doi.org/10.1210/jc.2014-2555

Chen H, et al. The effects of outdoor air pollution on chronic illnesses. Mcgill J Med. 2009;12(1):58-64.

- Outdoor air pollution linked to chronic illnesses – threatens entire populations

Montreal Canada, Aug 2002 →

Elevated toxic metal burden affects all organ systems

Toxicity, Heavy Metals

Soghoian S, MD, et al
Department of Emergency Medicine, State University of New York Downstate Medical Center

Background: Heavy metal toxicity represents an uncommon, yet clinically significant, medical condition. If unrecognized or inappropriately treated, heavy metal toxicity can result in significant morbidity and mortality. The periodic table contains 105

"Nearly all organ systems are involved in heavy metal toxicity; however, the most commonly involved organ systems include the central nervous system, peripheral nervous system, gastrointestinal, hematopoietic, renal, and cardiovascular."

pneumonitis that occurs after exposure to metal fumes from cadmium, manganese, mercury, and nickel. These exposures are clinically indistinguishable from MFF in the early stages but tend to progress to ARDS and cause significantly more morbidity and mortality.

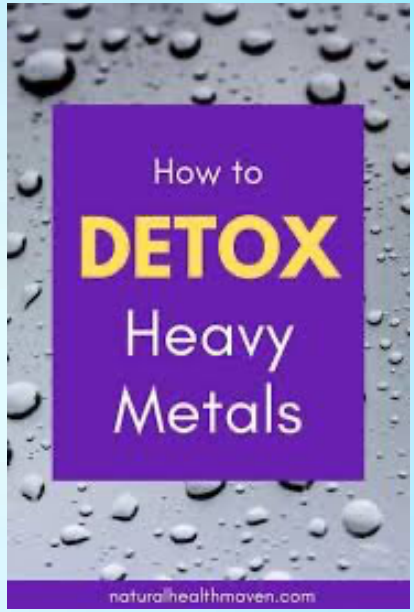
Toxic effects from chronic exposure to heavy metals are far more common than acute poisonings. Chronic exposure may lead to a variety of conditions depending on the route of exposure and the metabolism and storage of the specific element in question. For example, chronic exposure to cobalt dust has been associated with the development of pulmonary fibrosis that can lead to cor pulmonale. This hard metal pneumoconiosis has been described for other metal dusts. Chronic inhalation of high levels of cadmium also causes both fibrotic and emphysematous lung damage, but it also has major effects in bone and

http://www.emedicine.com/EMERG/topic237.htm

With permission from Henri Roca, MD

Metal Toxicity Mechanisms

- Denaturing enzymes
- Displace minerals in cells and tissues
- Interfere with cell membranes functions, ie transport, uptake and release
- Create free radicals/oxidative stress
- Induction of Inflammatory Cytokines
- Mitochondrial damage
- DNA damage

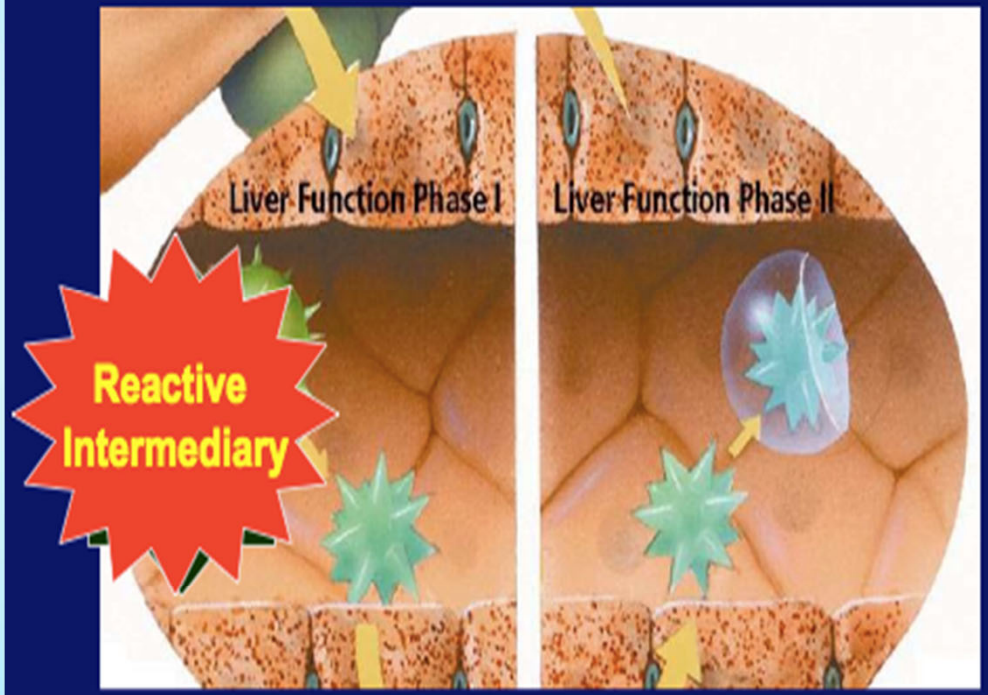


Clarkson TW. The three modern faces of mercury. Environ Health Perspect 2002;110:11-23

National Research Council. Toxicological Effects of Methylmercury. Washington, DC: National Academy Press 2000:31-70

Yee S, Choi BH. Oxidative Stress in Neurotoxic effects of methymercury poisoning. Neurotoxicology 1996;17:17-26

L-Cysteine, Magnesium and other nutrients support proper expression of Phase I CYP450 enzymes



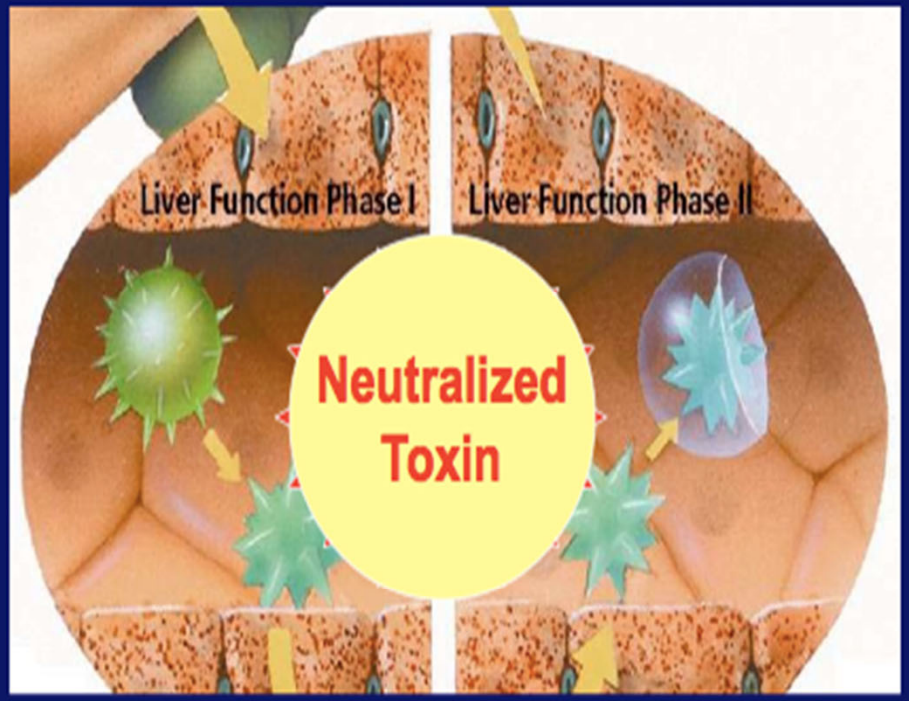
Phase I

Cytochrome P450 enzymes add reactive functional groups to fat-soluble toxins

Phase I
Functionalization

Phase II
Conjugation

Glycine, taurine, sodium sulfate and glutathione precursors support the creation of Phase II enzymes



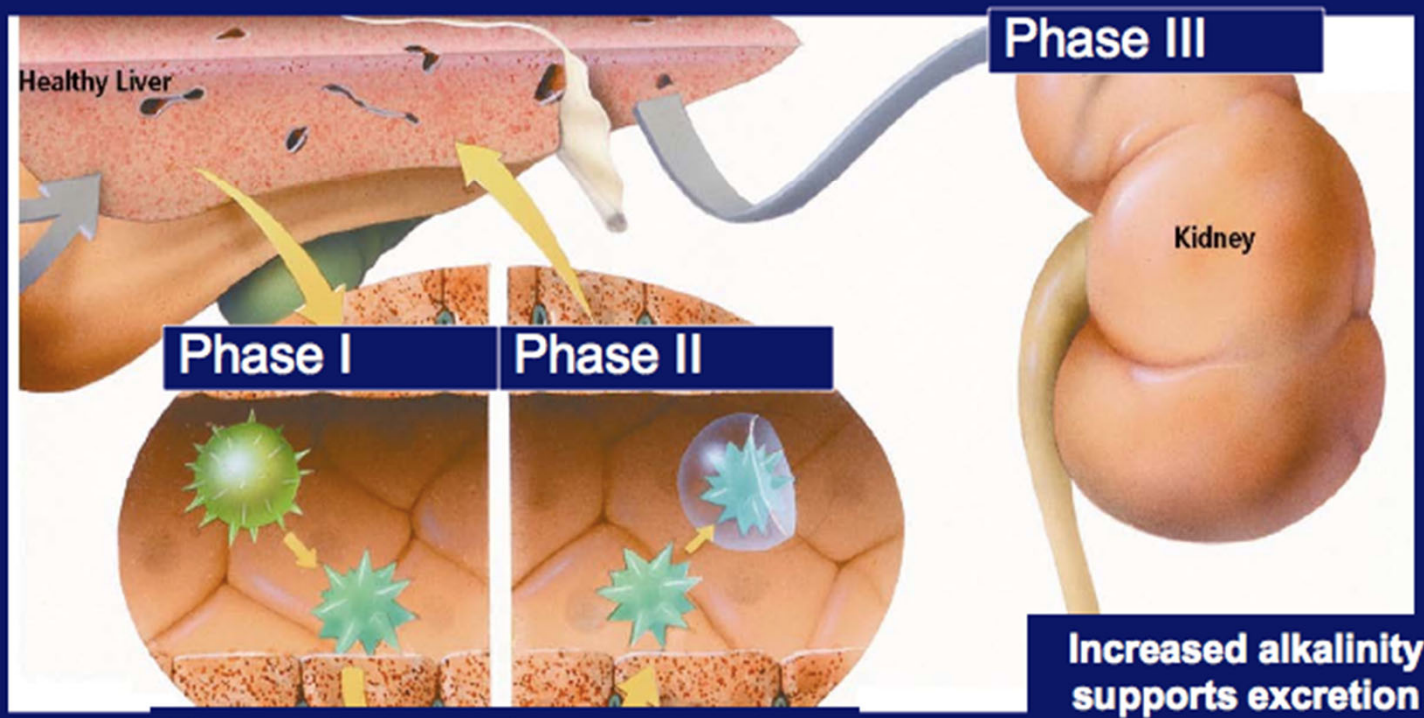
Phase I
Functionalization

Phase II
Conjugation

Phase II

The functional groups are then reacted with conjugation molecules to neutralize the toxins and make them water soluble

Metabolic detoxification improves the process of biotransformation and an alkaline urinary pH supports clearance of toxins



The Process of Detoxification and Elimination

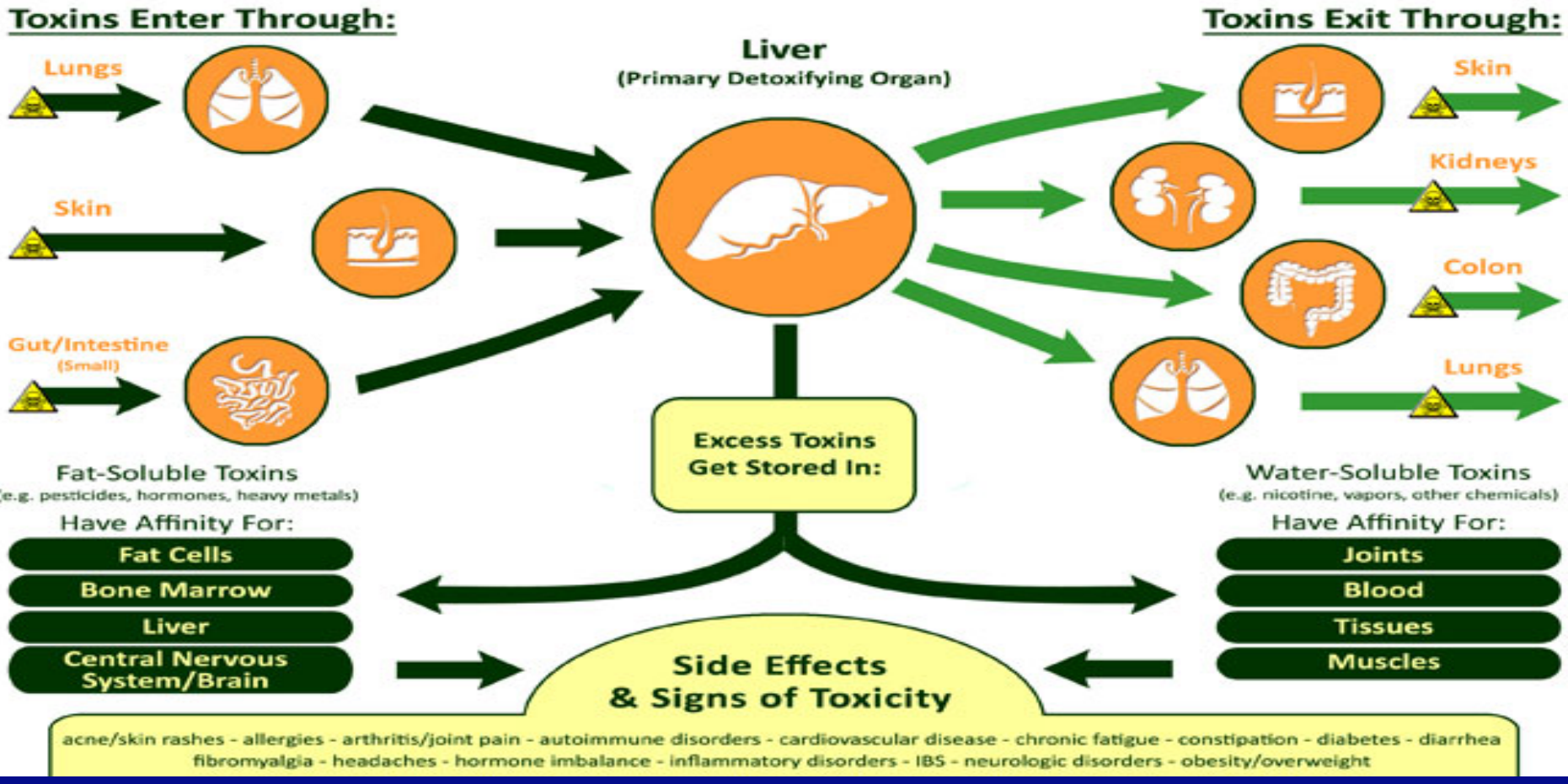
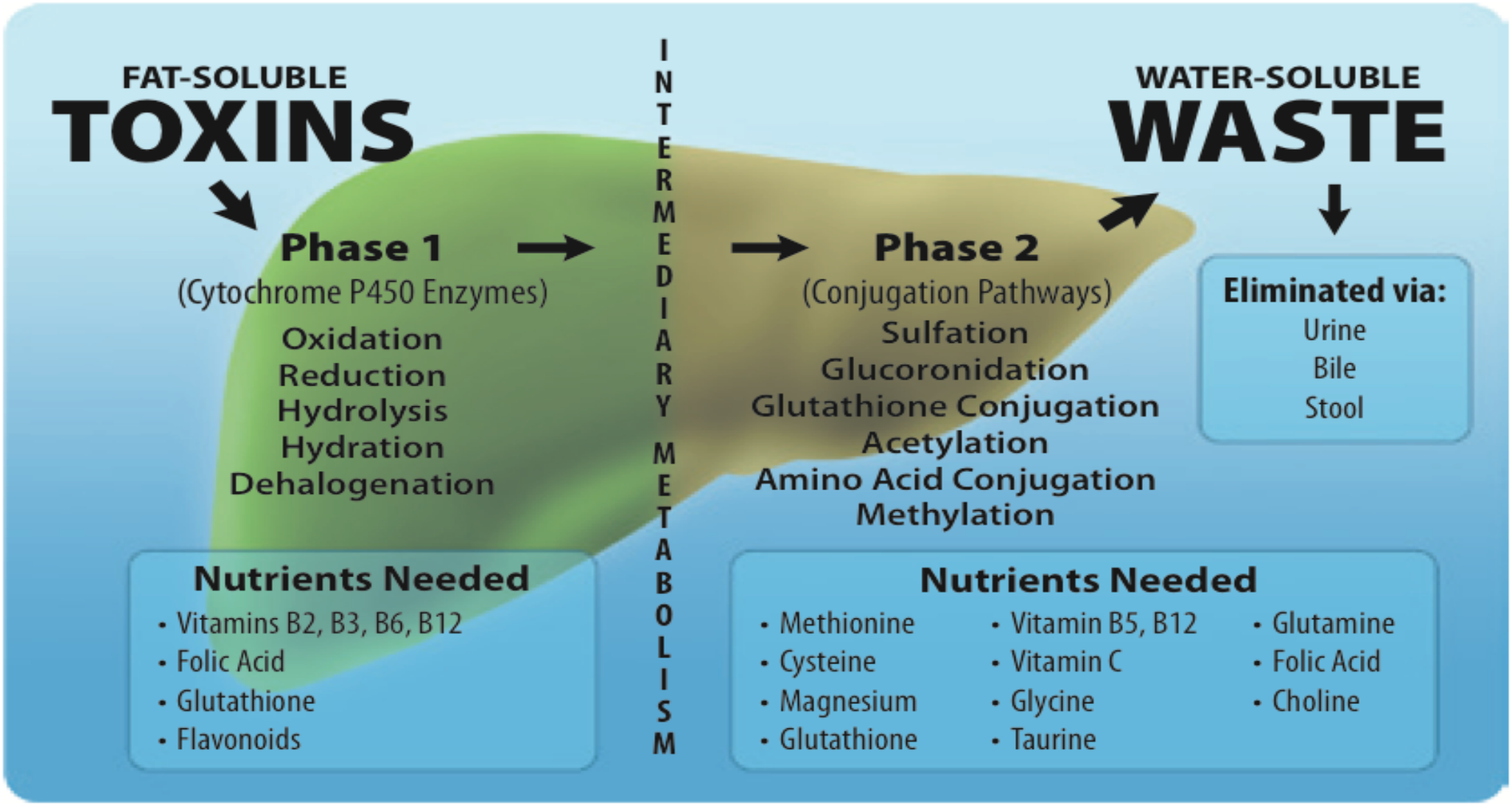


Figure 3. Phase I and II Liver Detoxification



Influencers of Phase I Detoxification

- **Factors that Speed Up Phase 1 Detoxification**
- Alcohol
- Caffeine
- St. John's Wort
- Drugs (sulfa, steroids, barbiturates
- Nicotine
- Pesticides

- **Factors that Slow Down Phase 1 Detoxification**
- Drugs (antidepressants, antihistamines, H2 blockers oral contraceptives)
- Trans Fats
- Grapefruit Juice
- Iron Overload

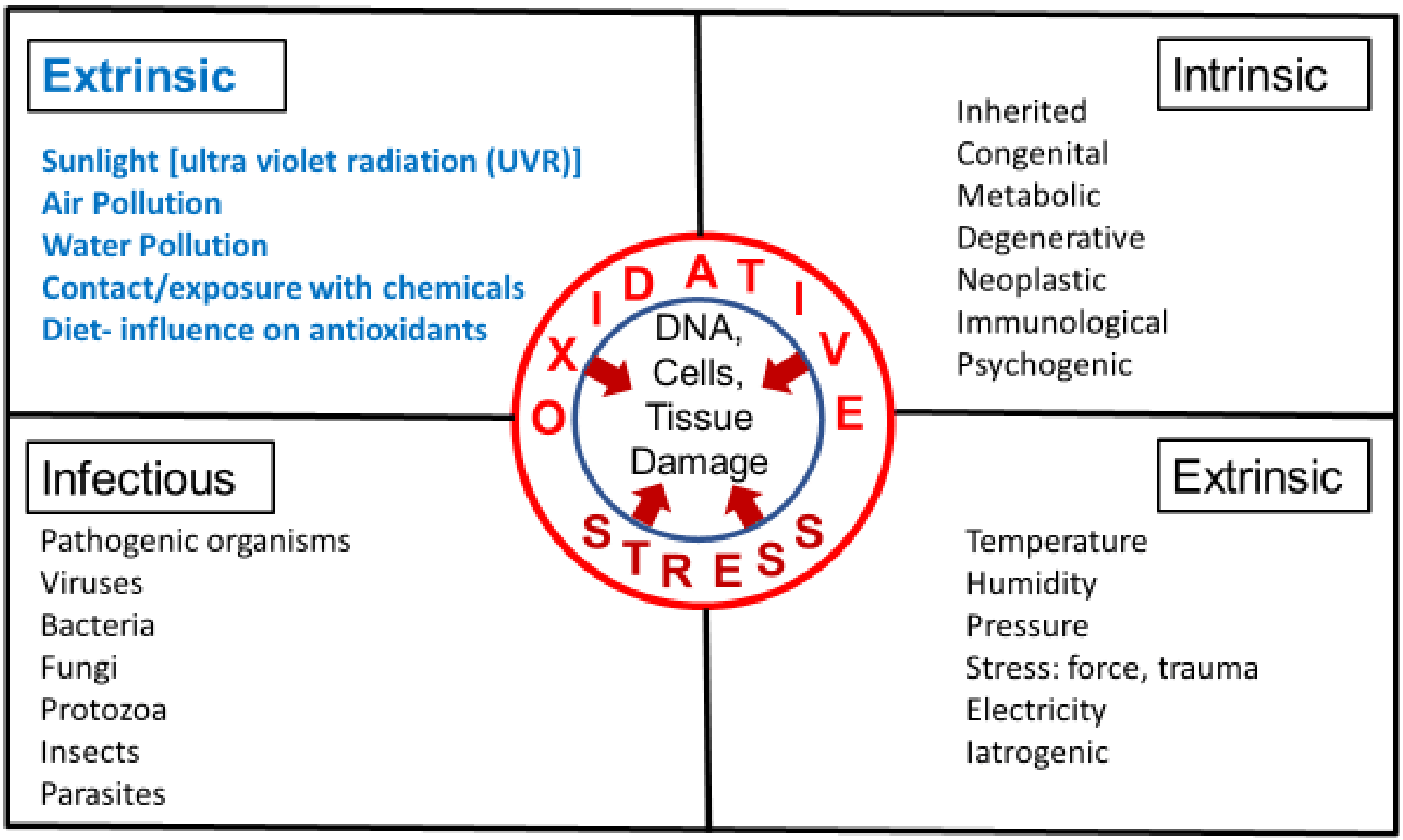
Influencers of Phase 2 Detoxification

Factors that Speed up Phase 2 Detoxification (desired)

- Cruciferous Vegetables
- Sulfurophane containing foods garlic, onions, leeks
- Limonene (from lemons)
- Milk Thistle

Factors that slow down Phase 2 Detoxification

- *Low Protein Diets*
- NSAID's
- Increased detox demand


Extrinsic
Sunlight [ultra violet radiation (UVR)]
Air Pollution
Water Pollution
Contact/exposure with chemicals
Diet- influence on antioxidants
Intrinsic
Inherited
Congenital
Metabolic
Degenerative
Neoplastic
Immunological
Psychogenic
OXIDATIVE STRESS
DNA, Cells, Tissue Damage
Infectious
Pathogenic organisms
Viruses
Bacteria
Fungi
Protozoa
Insects
Parasites
Extrinsic
Temperature
Humidity
Pressure
Stress: force, trauma
Electricity
Iatrogenic

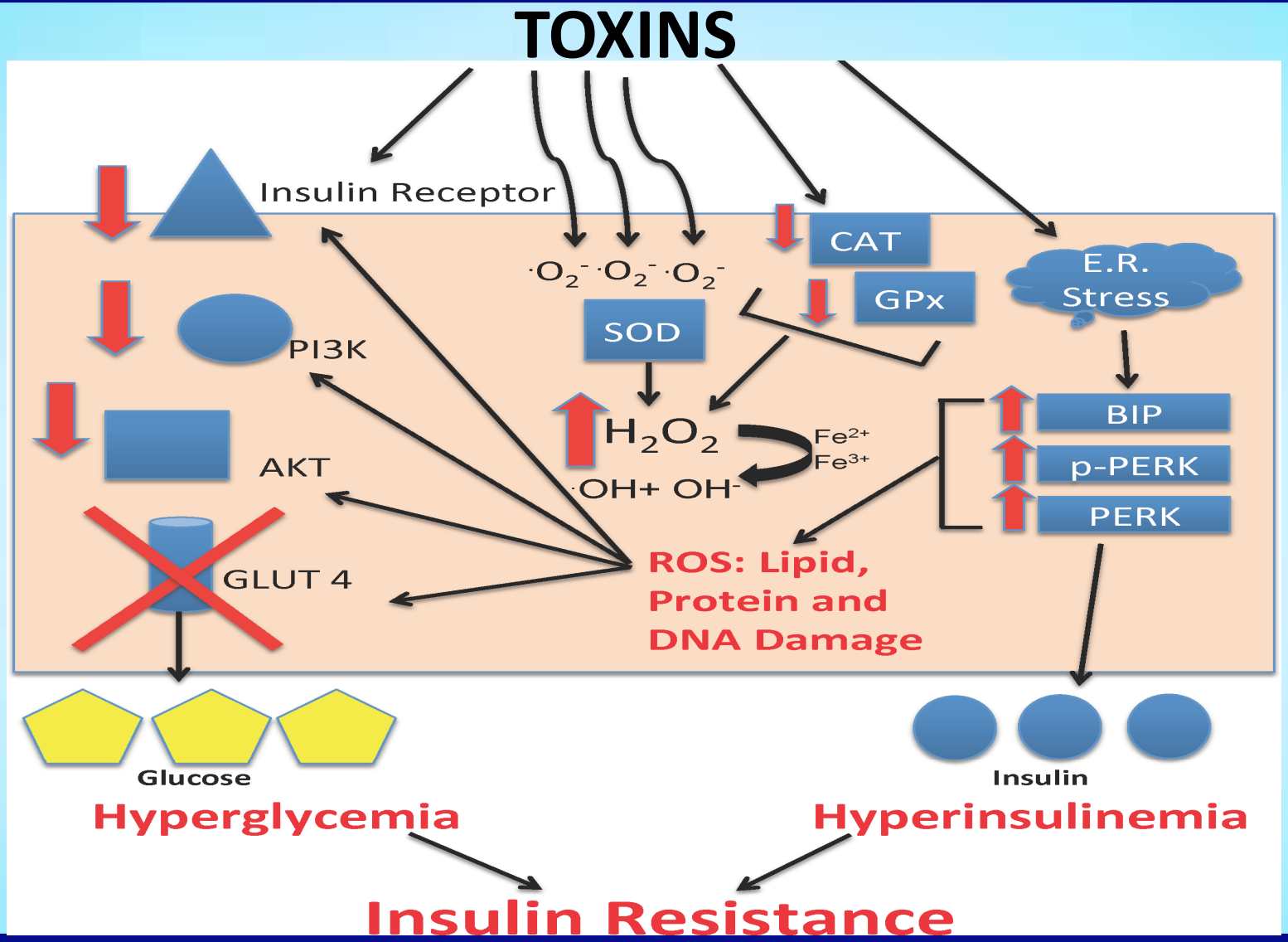
Environmental Toxins and IR

- Pesticides, BPA associated with increased risk for IR

- Heavy metals also associated with increased oxidative stress and inflammatory response

- Note - 90% of the pesticides in use today are used in the production of food

Ropero AB, et al. Bisphenol-A disruption of the endocrine pancreas and blood glucose homeostasis. Int J Androl. 2008 Apr;31(2):194-200.
Galanis A, Karapetsas A, Sandaltzopoulos R. Metal-induced carcinogenesis, oxidative stress and hypoxia signalling. Mutat Res. 2008 Oct 30.Lee DH, et al. Diabetologia. 2007 Sep;50(9):1841-51.


TOXINS
Insulin Receptor
PI3K
AKT
GLUT 4
$\cdot O_2^- \cdot O_2^- \cdot O_2^-$
SOD
CAT
GPx
H_2O_2
Fe^{2+}
Fe^{3+}
$\cdot OH + OH^-$
E.R. Stress
BIP
p-PERK
PERK
ROS: Lipid, Protein and DNA Damage
Glucose
Hyperglycemia
Insulin
Hyperinsulinemia
Insulin Resistance

Diabetes and Pesticide Exposure

- 33,457 licensed applicators, predominantly White non-Hispanic males
- Self-report, 1993-1997
- Two primary measures: ever use and cumulative lifetime use
- Seven pesticides identified
- Aldrin, Chlordane, Heptachlor – 51%, 63%, 94% odds ratio respectively

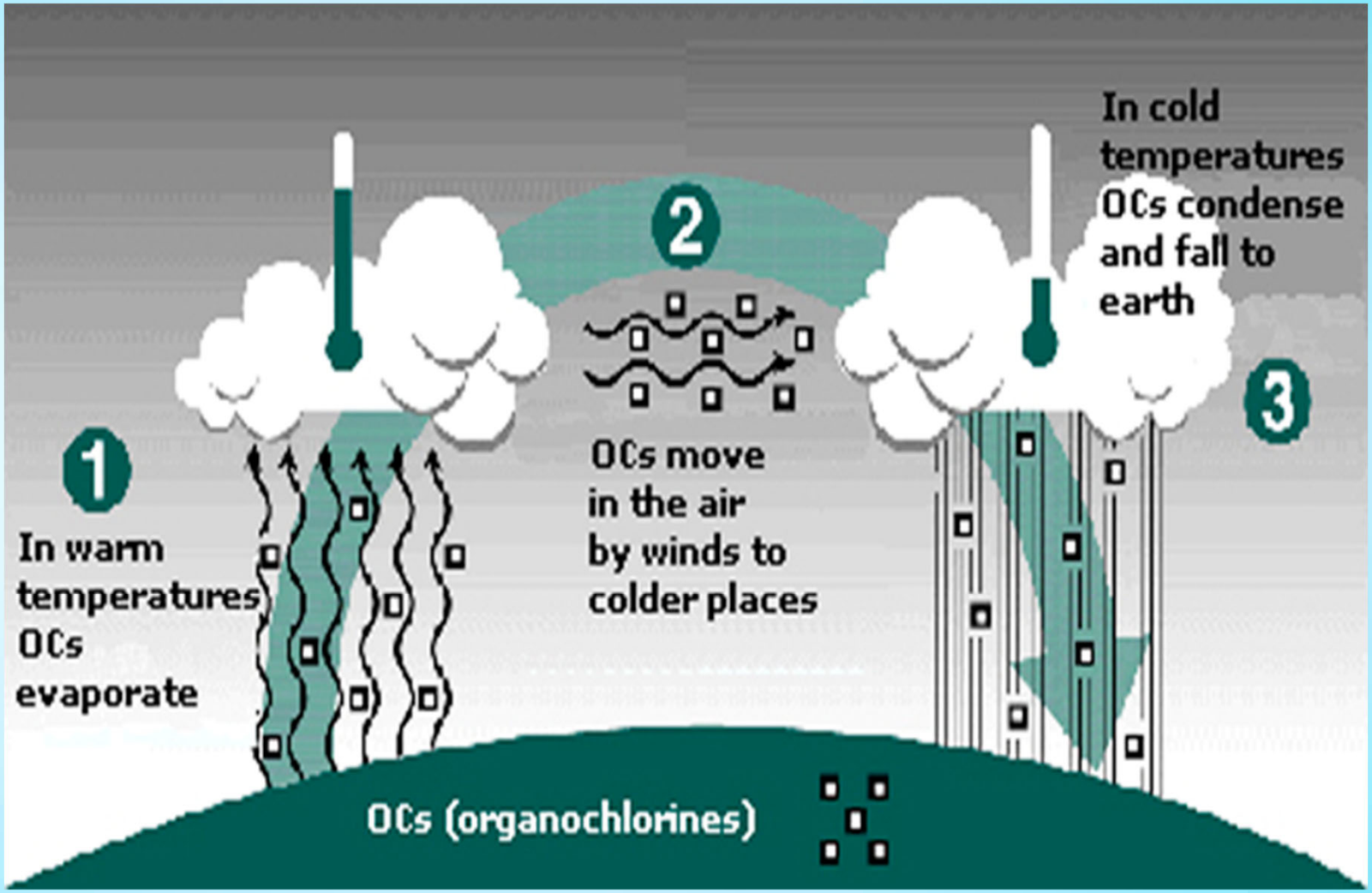
Montgomery MP, et al. Incident diabetes and pesticide exposure among licensed pesticide applicators: agricultural health study 1993-2003. Am J Epidemiol. 2008;167(10):1235-46.

Release of Toxins By Weight Loss

- Accumulation of lipophilic environmental toxins occurs in fat cells.
- Pesticides, including organochlorines, PCBs, heavy metals, and other compounds
- Weight loss increases the excretion of these toxins.
- Monitor patients on weight loss for signs of environmental toxicity.

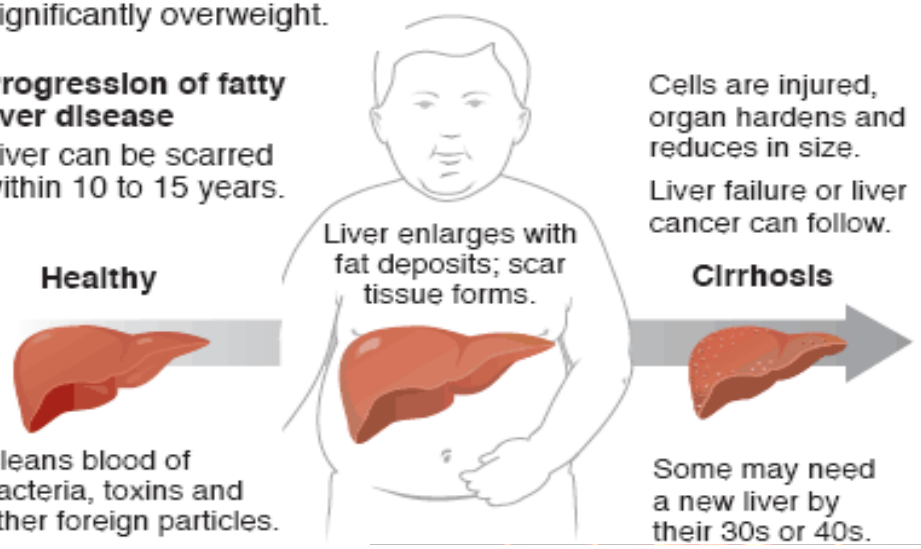
Jandacek RJ, Tso P.Lipids. Factors affecting the storage and excretion of toxic lipophilic xenobiotics.2001 Dec;36(12):1289-305. Review.

Organochlorines



Young, obese and at risk of disease

Experts estimate 2 to 5 percent of American children over age 5 have nonalcoholic fatty liver disease — nearly all of them significantly overweight.



SOURCES: American Liver Found

NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD)

- Food habits: eating high-fat concentrated, fried food with high cholesterol; "fast food"; sugar rich snacks.
- Lack or very low physical activity.
- Being overweight or obese.

Are you overloaded with toxins?

In the 21st century environmental toxins have increased dramatically – these include:

- **Multiple drug therapy & antibiotics**
- **Hormonal contraceptives, synthetic HRT & hormones in foods**
- **Fast food & processed food**
- **Over population of the planet leading to increased pollution**
- **Micro-waved & irradiated foods**
- **Plastics & dyes**
- **Heavy metals in our food & water**
- **Increased stress levels**
- **Increased alcohol consumption**
- **Smoking**

A healthy liver is your greatest protection against these things

JANUARY 29, 2020

Scientists have identified the role of chronic inflammation as the cause of accelerated aging

by Lobachevsky University

Lymphatic – Metaflammation Interplay

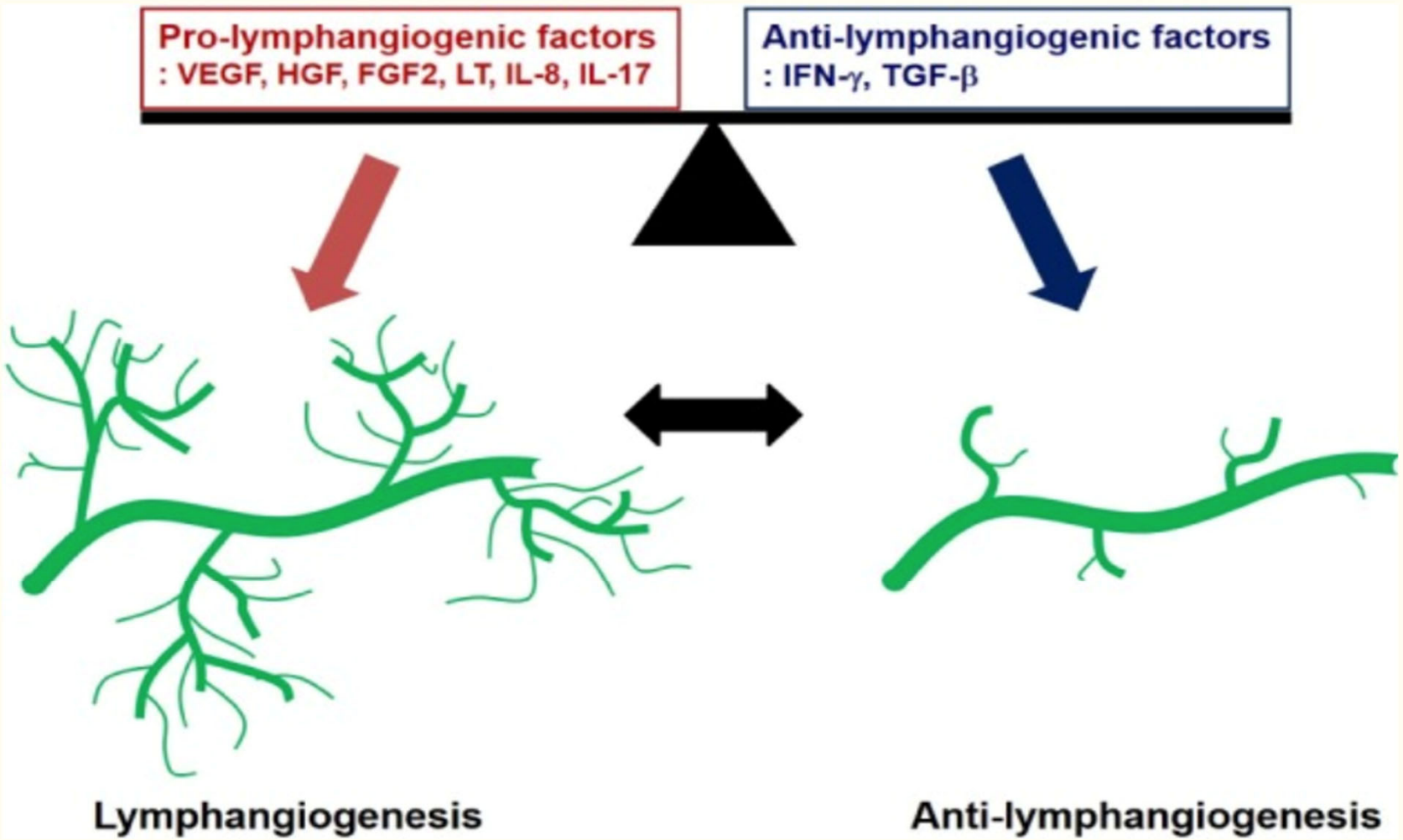
- Lymphatic vasculature has profound impact on inflammatory and immune responses
- Lymphatic vessels are routes for leukocyte migration
- Modulate fluid drainage
- Also active role in immune regulation
- Removal of inflammatory mediators from tissues

- Shin K, et al. Interplay between inflammatory responses and lymphatic vessels. Immune Network. 2014;14(4):182-86.
- Aebischer D, et al. The inflammatory respose of lymphatic endothelium. Angiogenesis. 2014;17(2):383-93.

Lymphatic – Metaflammation Interplay

- Tissue inflammation rapidly induces lymphatic endothelial cell proliferation and chemokine production
- Leads to lymphangiogenesis
- Lymphangiogenesis influences extent of inflammation
- Lymphatic endothelial cells induce T cell tolerance

Shin K, et al. Interplay between inflammatory responses and lymphatic vessels. Immune Network. 2014;14(4):182-86.



Shin K, et al. Interplay between inflammatory responses and lymphatic vessels. Immune Network. 2014;14(4):182-86.

6 THINGS YOU MAY NOT KNOW ABOUT LYMPHEDEMA

1 Lymphedema is chronic swelling caused by a build-up of fluid that occurs when the lymphatic system is either faulty or damaged.

Damaged vessels blocking the normal flow of lymphatic fluid

2 An estimated 3-5 million Americans suffer from lymphedema — including many that are undiagnosed or undertreated. *That is more than ALS, Cystic Fibrosis, Multiple Sclerosis, Muscular Dystrophy, and Parkinson's Disease combined.*

*2 out of 5 breast cancer patients will develop lymphedema within 5 years of surgery.**

3 Most physicians in the United States are taught about the lymphatic system for 1 hour or less during their 4 years of medical school training.

Swollen tissue due to buildup of lymphatic fluid

4 There is no known cure for lymphedema, but it can be effectively treated. Compression therapy is the most critical component of treatment. Without it, patients are at increased risk for complications and disability.

Causes of Lymphatic Dysfunction

A. Lymph node removal for cancer treatment
B. Injury to lymphatic vessels due to trauma or infection
C. Venous insufficiency, causing overload of lymphatic vessels
D. Congenital malformation of lymphatics

5 Medicare, and many private insurance policies do NOT cover compression garments, wraps, or bandages — the supplies needed for compression therapy.

6 The **Lymphedema Treatment Act** is a bill, currently in Congress, that aims to improve insurance coverage for compression supplies, allowing lymphedema patients to maintain a healthy and productive life.

LYMPHEDEMA TREATMENT ACT

Visit our website to learn more about lymphedema and how to support this bill.

LymphedemaTreatmentAct.org

**Journal of Clinical Oncology – J Clin Oncol. 2009 Jan 20;27(3):390-7.*

Inflammasomes

- Family of proteins in charge of the initiation of inflammatory process during innate immune response
- Pattern recognition receptors – stress, danger
- Major actors in metaflammation construct
- Signaling platforms associated with stress and damage
- No drug on the market targeting these proteins
- Most characterized = $NLRP_3$ nucleotide-binding domain leucine-rich repeat

Zahid A, et al Pharmacological inhibitors of the NLRP3 inflammasome. Front Immunol. 2019;2019:02538

GUT-LIVER AXIS

- GUT connects the liver w/ intestines via bile acid metabolism
- Bile acid (BA) dysregulation leads to intestinal dysbiosis
- Allows Gram (-) enterogenous pathogenic bacteria and LPS to enter liver via portal vein
- Triggers hepatic inflammation via inflammasomes

Wang J, et al. Roles of the inflammasome in the gut-liver axis. Mol Mol Rep. 2019;19(1):3-14.

GUT-LIVER AXIS

- **Decreased** Bile acids (BAs) in the gut lead to intestinal dysbiosis
- Impairs intestinal barrier function – lead to leaky gut
- Induces bacterial translocation to allow pathogens i.e. *Bacteroidetes* (Gram-negative bacteria) and LPS into the liver
- Aggravates hepatic inflammation
- Loss of intestinal epithelial stemness also contributes to bile duct ligation-induced cholestatic liver injury

Wang J, et al. Roles of the inflammasome in the gut-liver axis. Mol Mol Rep. 2019;19(1):3-14.
Sabino J, Vieira-Silva S, Machiels K, Joossens M, Falony G, Ballet V, Ferrante M, Van Assche G, Van der Merwe S, Vermeire S, Raes J. Primary sclerosing cholangitis is characterised by intestinal dysbiosis independent from IBD. Gut. 2016;65:1681–1689.

GUT-LIVER Inflammasomes

- Inflammasomes mediate innate immunity in liver / GUT
- (NLRP)6 protein dominant in intestinal microbial balance
  - Via NACHT, LRR and PYD domains
- Promotes IL-18-dependent antimicrobial peptide (AMP) synthesis
- Promotes mucus secretion from goblet cells

Wang J, et al. Roles of the inflammasome in the gut-liver axis. Mol Mol Rep. 2019;19(1):3-14.

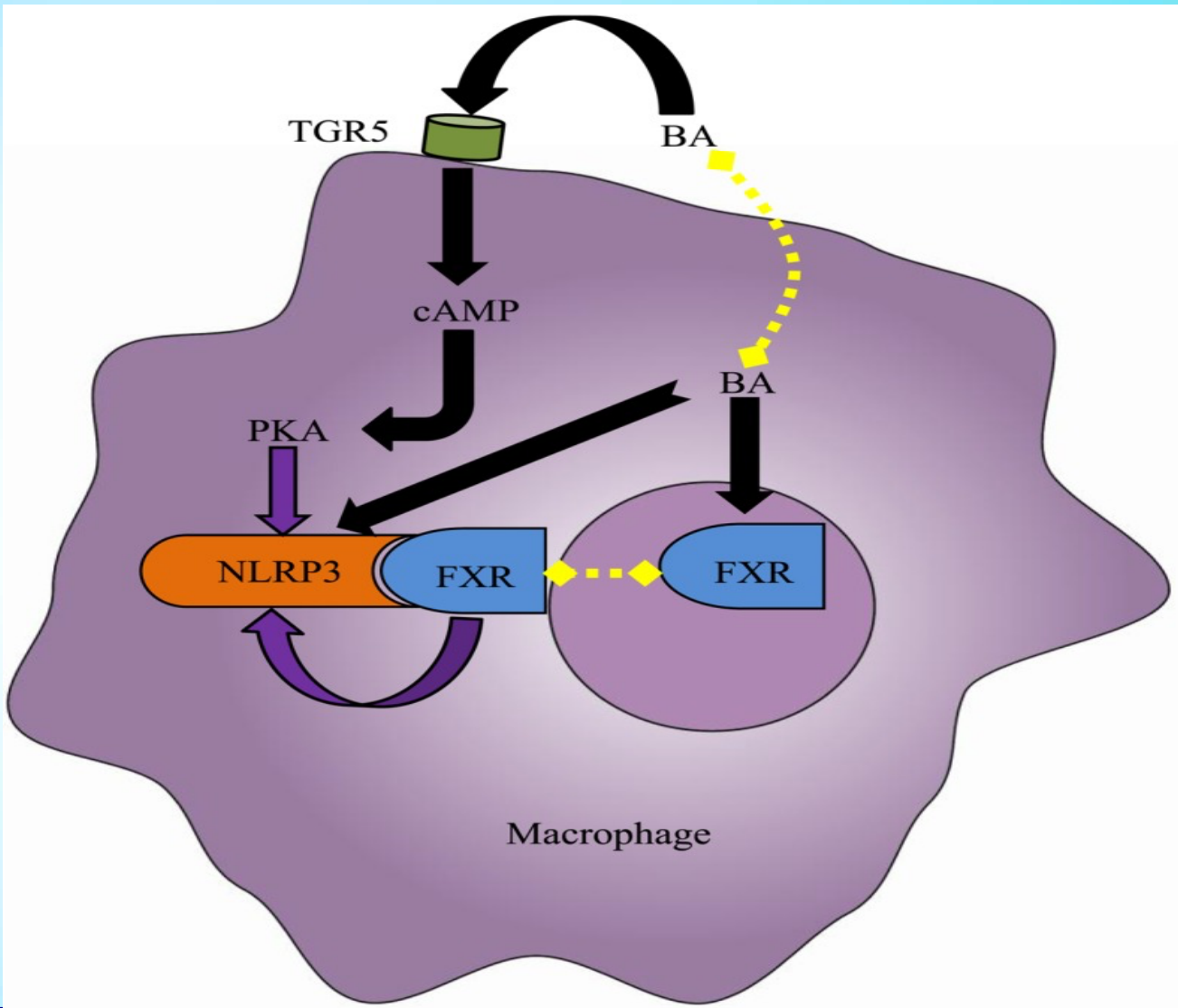
GUT-LIVER Inflammasome Interaction

- In contrast, NLRP3 inflammasome primarily induces IL-1beta

- BAs activate NLRP3 inflammasome in macrophages
  - Aggravates inflammatory liver injury
  - Affects the epithelial integrity of cholangiocytes by inducing the production of pro-inflammatory cytokines
  - Excessive Bas induce hepatocyte death

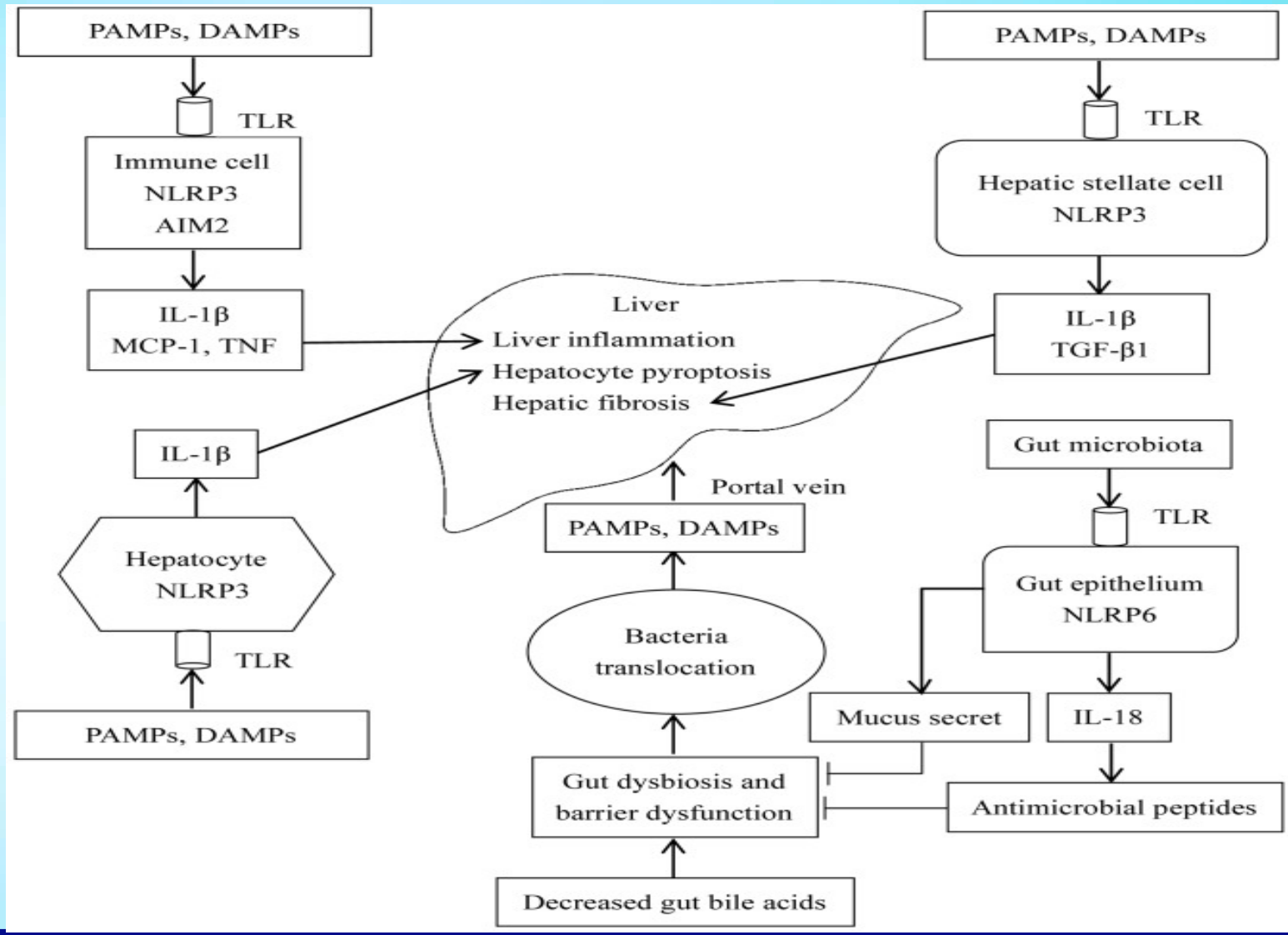
Wang J, et al. Roles of the inflammasome in the gut-liver axis. Mol Mol Rep. 2019;19(1):3-14.

Bile Acid Effects on NLRP3 Inflammasome in Macrophage



Wang J, et al. Roles of the inflammasome in the gut-liver axis. Mol Mol Rep. 2019;19(1):3-14.

Role of Inflammasome in GUT-LIVER Axis



Wang J, et al. Roles of the inflammasome in the gut-liver axis. Mol Mol Rep. 2019;19(1):3-14.

EH3

Slide 40

EH3 Ernie Hawkins, 9/17/2020

GUT-LIVER Axis Study

- 2011 2-part cohort study
  - 2754 IBD patients
  - 82 primary sclerosing cholangitis (PSC)
- RESULTS:
- An inflamed colon is important in PSC development
- Bacterial translocation and subsequent portal bacteremia is important in PSC development in IBD

O'Toole A, Alakkari A, Keegan D, Doherty G, Mulcahy H, O'Donoghue D. Primary sclerosing cholangitis and disease distribution in inflammatory bowel disease. Clin Gastroenterol Hepatol. 2012;10:439–441.

An Emerging Health Target: Managing pH of your intracellular fluids

- The more acidic you are the more oxidative stress you are under
- Oxidative Stress is the rate of rusting you are undergoing.
- pH is essential to cellular health
- Acidic chemistry leads to lactate build up, cellular damage and is associated with the development of “immortal cells”
- pH is highly dependent on hydration and micronutrient content from fruits and vegetables(particularly vegetables).
- Magnesium and Potassium being key

THE "ACIDOSIS" CYCLE

Eat & Drink ACIDIC Substances
Little or No Exercise
Poor Digestion
Poor Bowel Elimination

Tissues and organs become ACIDIC and rob calcium from bones to neutralize acidity. Calcium deposits develop in fatty acidic tissues (e.g. breasts)

Bones are "shorted" of calcium
Weak/brittle/porous bones

Acidosis in body causes:
- poor health
- chronic illness
- cancer
- osteoporosis
- arthritis
- blocked lymph nodes
- inadequate perspiring

& hundreds more ! !

Low –Grade Acidosis Cycle

Poor Nutrition, Stress, Toxins, Medications, Poor Digestion

Low-Grade Acidosis Causes:

Fatigue, insulin resistance, weight gain, muscle and joint pains, irritable bowel syndrome, acid reflux, bone loss, muscle wasting,
Skin problems, receding gums, memory loss, kidney disorders, chronic disease

Acid Waste Accumulates in the Cells, Tissues and Organs

The Body has Buffering Systems

The body tries to buffer the acid waste, but it becomes overwhelmed with it. Eventually the acid waste is store inside the body

The Cycle of Optimal Health

70 to 80% Alkaline Foods 20 to 30% Acid Foods

pH Balance

pH Balance Prevents Disease:
Decreasing the risk for Diabetes, Bone Loss, Heart Disease, Cancer and other Chronic Disease

pH Balance Promotes:
Flexible cell membranes enabling efficient uptake of vitamins, minerals, phytochemicals and oxygen into the cells.

pH Balance Controls the Body Self Healing
The body's repair systems work efficiently in a pH balanced environment. The result: Stronger immune system, efficient detoxification .


COLA
Energy Drink
Purified Water
Tap Water
Sea Water
3
4
5
6
Acidic
7
Neutral
8
Alkaline
9
10
pH
Acidic
pH SPECTRUM
Alkaline
pH

Redox & Renal Function

- Loss of redox homeostasis and heightened free radical activity is at the heart of kidney disease and
- Loss of redox pois accounts for proinflammatory pro-fibrotic activation.
- Leads to renal hypertension

Lombo-Garza C, et al. Redox homeostasis, oxidative stress, mitophagy. Mitochondrion. 2020;51:105-117.

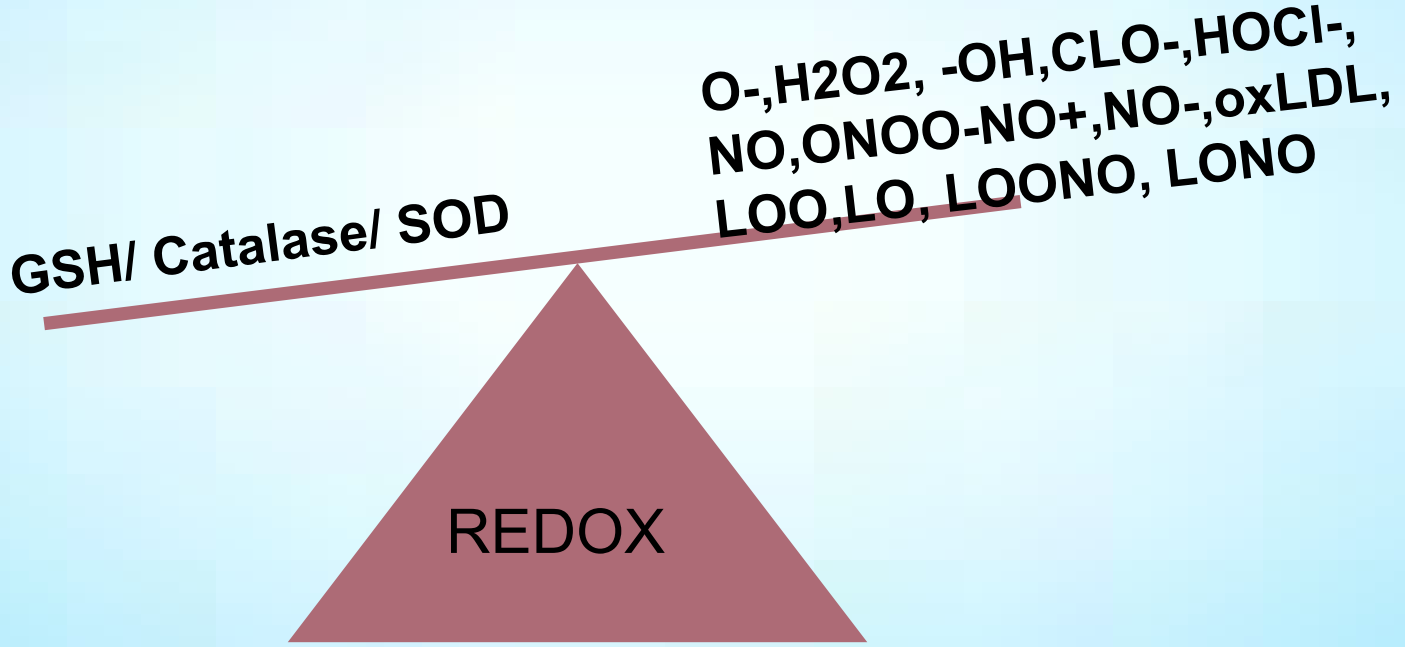
Chronic Renal Failure CKD

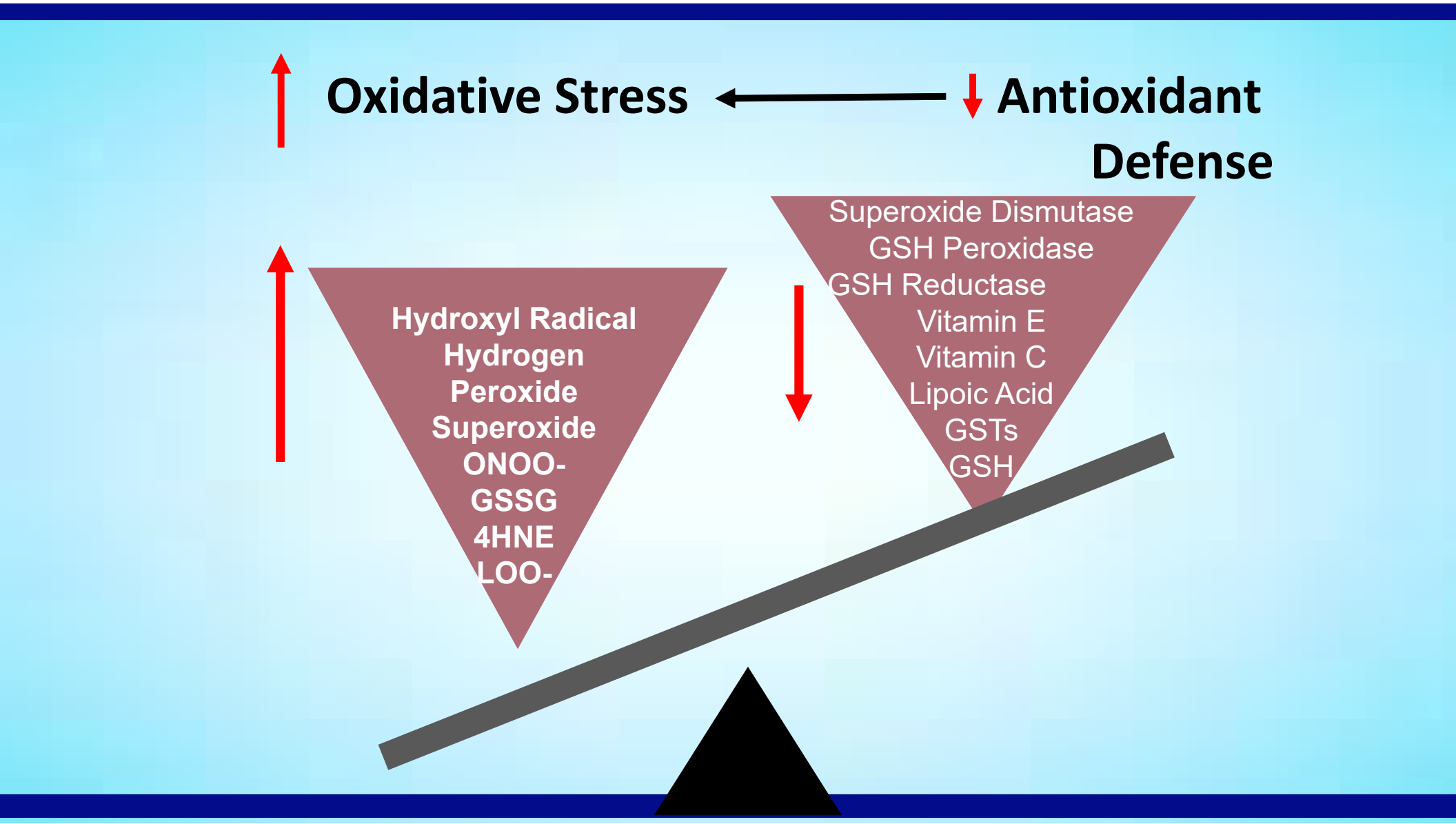
- Associated with Oxidative Stress and increased ROS in the Nephrons
- Decreased Glutathione, SOD, Catalase
- Melatonin decreased ROS species and improved renal blood flow in rat model
- Approx. 37 million people in US have CKD – approximately 90% of these don't know they have it

CDC. www.cdc.gov. Accessed Feb 2020

Goksel;Paskalolatin et al Metaltonin ameliorates chronic renal failure induced oxidative organ damage in rats, Journal of Pineal Research 36(4):232-241, May 2004

Redox Balance = Rate of Rusting




Oxidative Stress
Antioxidant Defense
Hydroxyl Radical
Hydrogen Peroxide
Superoxide
ONOO-
GSSG
4HNE
LOO-
Superoxide Dismutase
GSH Peroxidase
GSH Reductase
Vitamin E
Vitamin C
Lipoic Acid
GSTs
GSH

Low Urinary pH

Linked to:

- Accumulation of Visceral fat
- IR
- Methylglyoxal concentration
- Hypertension
- Increased intrarenal oxidative stress
- Up-regulation of renin-angiotensin system
- Low levels of growth hormone

Ogawa S, Takiguchi J, Nako K, et al. Elucidation of the etiology and characteristics of pink urine in young healthy subjects. Clin Exp Nephrol 2014. Published Online First. doi:10.1007/s10157-014-1066-y

Alkalinize to Spare the Kidneys

- Bicarbonate has been used to reduce the need for dialysis
- Alkalinization can suspend proteinuria-induced oxidative damage (proximal tubular cells)
- Lower UpH reinforces oxidative stress via albumin reabsorption (tyrosine kinase 2)
- Also correlated to intimal medial Thickness (IMT)
- Independent correlations to UpH and progression UA serum, Ankle brachial plexus index, EGFR, heart rate and number of RASI's taken.

Souma T, Abe M, Moriguchi T, et al. Luminal alkalinization attenuates proteinuria-induced oxidative damage in proximal tubular cells. J Am Soc Nephrol 2011;22:635–48.

Basic Concept pH and Progression of Renovascular Disease

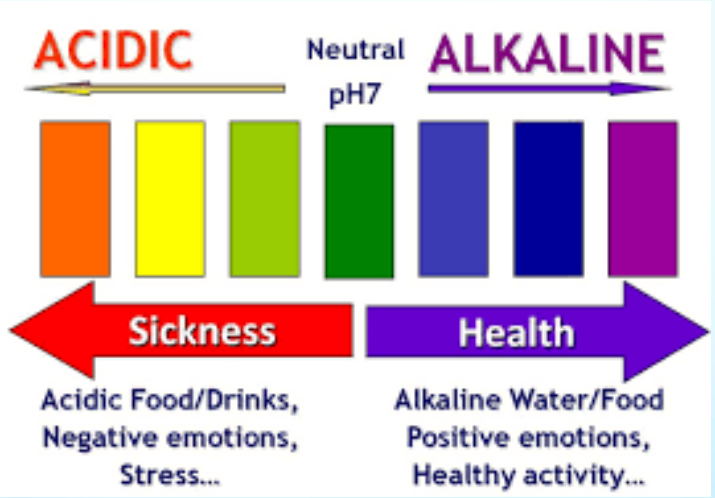
- Lower Urinary pH Is Useful for Predicting Renovascular Disorder Onset in Patients With Diabetes
- Study n= 300 patients over 10 years tracked
- UpH negative correlation with deoxyguanosine
- UpH a useful and predictive marker for onset of renovascular disease in people with diabetes
- Aids precipitation of uric acid
- Also common issue in CKD and Obesity

Susumu Ogawa; Kazuhiro Nako; Masashi Okamura; Sadayoshi Ito BMJ Open Diabetes Res Care. 2015;3(1)
Katsiki N, Papanas N, Fonseca VA, et al. Uric acid and diabetes: Is there a link? Curr Pharm Des 2013;19:4930–7.

Study Conclusion

- Over a decade improvements in BG, Lipids and BP occurred with drug therapy
- Number of drugs went up significantly in the trial
- NO improvements were seen in obesity, acidosis, fatty liver, hyperuricemia Nor could advancement of renovasuclar disease be halted
- Lower UpH also directly correlates the need for RASI's.
- Study follows findings in previous non-diabetic population.

How Do You Alkalinize pH?



Plant based alkaline diet

- Excess dietary protein with high acid renal load may decrease bone density if not buffered by ingestion of supplements or foods that are alkali rich

- A three-year study looking at a diet rich in potassium, such as fruits and vegetables, as well as a reduced acid load, resulted in preservation of muscle mass in older men and women

- Alkaline diet reported to help improve pain

Schwalfenberg GK. The alkaline diet: Is there evidence that an alkaline pH diet benefits health? J Environ Public Health. 2012;2012:72630.

Increasing Plants in the Diet

- 2019 clinical study using 168 individuals in the ARIC (Atherosclerosis Risk in Communities) study
- Followed patients from 1987 – 2016
- Those adhering to an overall plant-based diet index or provegetarian diet had:
  - 16% lower risk of cardiovascular disease
  - 32-32% lower risk of cardiovascular disease mortality
  - 18-25% lower risk of all cause mortality

Kim H, et al.Plant-based diets are associated with a lower risk of incident cardiovascular disease, cardiovascujlar disease mortality and all cause mortality in a general population of middle–aged adults. J Am Heart Assoc. 2019;8:e012865.

Intake of Vegetables, Fruit and Legumes

- **Fruit, vegetable, and legume intake, and cardiovascular disease and deaths in 18 countries (PURE): a prospective cohort study.**

- Higher fruit, vegetable, and legume consumption was associated with a lower risk of non-cardiovascular, and total mortality. Benefits appear to be maximum for both non-cardiovascular mortality and total mortality at three to four servings per day (equivalent to 375-500 g/day).

- Lancet. 2017 Nov 4;390(10107):2037-2049. doi: 10.1016/S0140-6736(17)32253-5. Epub 2017 Aug 29.

Supplement Support for Liver-Lymph-Kidney Axis

- Improves all phases of liver detoxification
- Improves liver antioxidant system
- Supports kidneys, improves flow
- Decreases kidney oxidative stress
- Supports lymphatic flow and drainage

Goldenrod (*Solidago virgaurea*)

- German Commission E monographs lists European goldenrod as an agent for Kidney and Bladder disorders
- Considered an “aquaretic” vs. synthetic diuretic
- Mild effects
  - Increases renal blood flow
  - Increases the glomerular filtration rate without stimulating the loss of sodium and chloride
  - Antioxidant
  - Antibacterial effect

Melzig MF. [Goldenrod – a classical component in the urological phytotherapy]. Wein Med Wochenschr. 2004;154(21-22):523-7.
El-Tantawy WH. Biochemical effects of Solidago virgaurea extract on experimental cardiotoxicity. J Physiol Biochem. 2013;[Epub ahead of print].
Starks CM, Williams RB, Goering MG, et al. Antibacterial clerondane diterpenes from Goldenrod (Solidago virgaurea). Phytochemistry. 2010;71(1):104-9.
Leuschner J. Anti-inflammatory, spasmolytic and diuretic effects of a commercially available Solidago gigantean Herb. Extract. Arzneimittelforshung. 1995;45(2):165-8.

Goldenrod (*Solidago virgaurea*)

- Used in EU for:
  - Lower urinary tract irrigation
  - Especially in cases of inflammation and renal calculi
  - And in infections of urinary tract

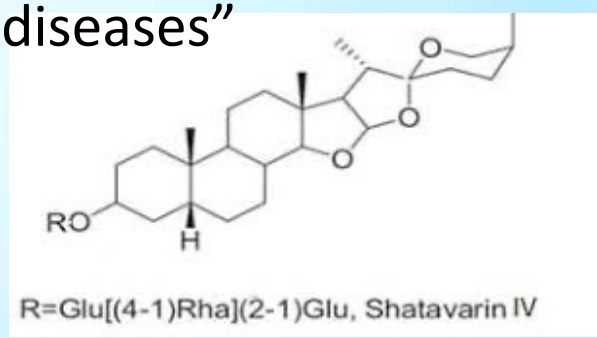
- 500mg BID 4:1 extract

Braun, R. et al. 1997. *Standardzulassungen f r FertigarzneimittelText and Kommentar.* Stuttgart: Deutscher Apotheker Verlag.

British Herbal Pharmacopoeia (BHP). 1996. Exeter, U.K.: British Herbal Medicine Association. 9091.

Shatavari (*Asparagus Racemosus*) stems

- Ayurvedic herb used for thousands of years as “diuretic” and tonic
- Used traditionally in Sri Lanka, Himalayas and India
- Shatawari means “curer of a hundred diseases”
- Phytochemicals include shatavarin and other steroidal saponins



R=Glu[(4-1)Rha](2-1)Glu, Shatavarin IV

Alok S, et al. Plant profile, phytochemistry and pharmacology of Asparagus racemosus (Shatavari): a review. Asian Pac J Trop Dis. 2013;3(3):242-51

Shatavari (*Asparagus Racemosus*) stems

- Immune Modulation
- Mixed Th1/Th2 immune activity
- Modulates inflammatory cytokine release – TNF alpha, IL-1beta
- Nephroprotective/antilithiatic effect
- Antioxidant/Anti-inflammatory
  - Protects from lipid peroxidation

Alok S, et al. Plant profile, phytochemistry and pharmacology of Asparagus racemosus (Shatavari): a review. Asian Pac J Trop Dis. 2013;3(3):242-51
.

Shatavari (*Asparagus Racemosus*) stems

- 2011 double-blind, placebo-controlled study
- n= 60 lactating mothers
- Administered sharavari orally – prolactin levels evaluated
- Reported to increase increase prolactin levels 3 x over placebo
- Milk production in humans 3x control
- Authors conclude Shatavari root is a galactagogue
- 250mg BID std to 40-50% shatavarins

Alok S, et al. Plant profile, phytochemistry and pharmacology of Asparagus racemosus (Shatavari): a review. Asian Pac J Trop Dis. 2013;3(3):242-51
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Dandelion (*Taraxicum officinale*)

- Liver and kidney “Tonic”
- Nutritive plant – rich source of beta-carotene, Vitamin A, Vitamin K, vitamin C, D, E, B vitamins, calcium, potassium
- One of richest vegetable sources of Beta-carotene – same as carrots (11,000 ug/100gm plant material)
- Roots high in inulin (prebiotic, up to 45% root), carotenoids (lutein), fatty acids, minerals, sugars, choline, mucilage and pectin
- Leaf diuretic
- Antioxidant, anti-inflammatory – chicoric acid, chlorogenic acid, taxasterol

Sumanth M. Rana A. In vivo antioxidant activity of hydro-alcoholic extract of Taraxacum officinale roots in rats. Indian J Pharmacol. 2006;38 pNA.
Trojanova I, Rada V, Kokoska L, et al. The bifidogenic effect of Taraxacum officinale root. Fitoterapia. 2004;75(7-8):760-3.
Hook I. McGee A. Henman M. Evaluation of dandelion for diuretic activity and variation in potassium content. Int J Pharmacog. 1993;31:29–34.

Dandelion (*Taraxicum officinale*) root

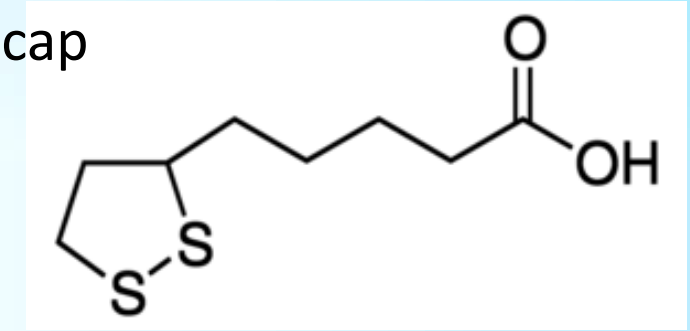
- Taxasterols also cholerectic – increase bile secretion
- Inulin is prebiotic FOS
  - Acts to improve microfloral diversity
  - Improves bifido bacteria most
  - Helps improves blood glucose levels
  - Supports beta cell dysfunction
  - Improves insulin secretion and sensitivity
  - Improves glucose update in muscle cells
- 200mg BID 4:1 extract

Tousch D, et al. Chicoric acid, a new compound able to enhance insulin release and glucose uptake. Biochem Biophys Res Commun. 2008 Dec 5; 377(1):131-5.

Trojanova I, Rada V, Kokoska L, et al. The bifidogenic effect of Taraxacum officinale root. Fitoterapia. 2004;75(7-8):760-3.

ALA Alpha Lipoic Acid

- Alpha lipoic acid, mixed racemic = 300mg / cap
- AKA thioctic acid
- Antioxidant
- Anti-metaflainflammatory
  - Decreases Th1 mediated inflammatory processes
- Cardio and Renal supportive



Zhang J, et al. Lipoic acid in the prevention of acute kidney injury. Nephron. 2016;134:133-140.
Merida S, et al. Free Radic Res. 47(8):593-601.

Alpha Lipoic Acid (ALA)

- Decreases diabetes complications – oxidative stress induced
- Reported to improve insulin sensitivity
- Improved glycemic control
- Reduced incidence/symptoms of neuropathies

Padmalayam I, et al. ipoic acid synthase (LASY): a novel role in inflammation, mitochondrial function, and insulin resistance. Diabetes. 2009 Mar;58(3):600-8.

ALA Mechanisms

- Naturally occurring lipoic acid = lipollysine
  - High levels in Spinach, Broccoli, tomatoes
  - ALA reduced to dihydrolipoic acid (DHLA) intracellularly
- Both ALA and DHLA act as a free radical scavenger of ROS and RNOS in vivo
- Mechanisms related to the phosphatidylinositol 3-kinase/Akt/Nrf2 pathway and the PI3-kinase/Akt pathways
  - Cell survival
  - Myocardial preconditioning
  - Myocardial contractility
  - Antiinflammation

Zhang J, et al. Lipoic acid in the prevention of acute kidney injury. Nephron. 2016;134:133-140.

ALA Mechanisms

Proposed Mechanisms:

- Improve glucose and ascorbate handling
- Increase endothelial nitric oxide synthase activity
- Activate phase II detoxification via the transcription factor Nrf2
- Lower expression of matrix metalloproteinase-9 and vascular cell adhesion molecule-1 through repression of nuclear factor-κB (NF-κB)
- Metal chelation/detoxification

Biewenga GP, Haenen GR, Bast A: The pharmacology of the antioxidant lipoic acid. Gen Pharmacol 1997; 29: 315–331.

ALA Mechanisms

- Affects beta cell function
- ↑cAMP-activated protein kinase (AMPK)
- ↑ PGC-1 alpha, ↑ PPAR alpha
- Improves glucose utilization and mitochondrial biogenesis
- Studies report exercise and ALA therapy improves IRS-1 dependent insulin signaling

Henriksen EJ. Exercise training and the antioxidant alpha-lipoic acid in the treatment of insulin resistance and type 2 diabetes. Free Radic Biol Med. 2006 Jan 1;40(1):3-12. Review.

ALA Studies

- 2011, Double-blinded, randomized, placebo-controlled clinical trial
- N= 63 patients (ages 22-79) - **End Stage Renal Disease** undergoing maintenance hemodialysis (HD)
- Supplemented w/ ALA 600mg or placebo. X 8 weeks
- RESULTS:
  - **CRP-hs significantly decreased – av. 18.7%**
- Authors conclude: ALA supplementation significantly reduced hsCRP levels, which is a risk factor for cardiovascular disease in HD patients.

Khabbazi T, et al. Effects of alpha lipoic acid supplementation in inflammation, oxidative stress and serum lipid profile levels in patients with end stage renal disease on hemodialysis. J Renal Nutr. 2011;22(2):244-50.

ALA

- 2018 meta analysis of 12 trials
- ALA effects on weight/body mass
- Up to 1,200 mg daily
- RESULTS:
  - Slight but significant decrease in weight and BMI
  - ALA treatment 1.27 kg greater increase in wt loss over placebo

Namazi N, et al. Alpha lipoic acid supplement in obesity treatment: a systematic review and meta analysis of clinical trials. Clin Nutr. 2018;37(2):419-428.

ALA Dosage

- 1 capsule (300mg) - 2 times daily
- Higher dosages may be necessary depending on clinical presentation
    - Eg. 1,500mg daily for weight loss support

Liver Glandular Concentrate

- Supports hepatic function
- Decreases hepatic oxidative stress
- Improves fatigue
- New Zealand bovine liver tissue
- Lyophilized and freeze-dried leaving peptides and enzymes intact
  - Unlike desiccated that destroys sensitive protein bonds
- High level of SOD (superoxide dismutase) + Catalase enzymes
- Minerals/vitamins

Liver glandular concentrate

- Pernicious anemia
- Supports iron and ferritin for pre-workout
- Double-blind study of using liver extract for hepatic dysfunction
  - Assessed clinical changes eg. digestion, constipation, hepatomegaly, cholesterol, prothrombin, RBC and hemoglobin
  - Reported 60% patients improved vs. placebo
  - Lack of side effects
- 1 scoop = 2,000 mg liver **FREEZE-DRIED** tissue powder – use QD-TID

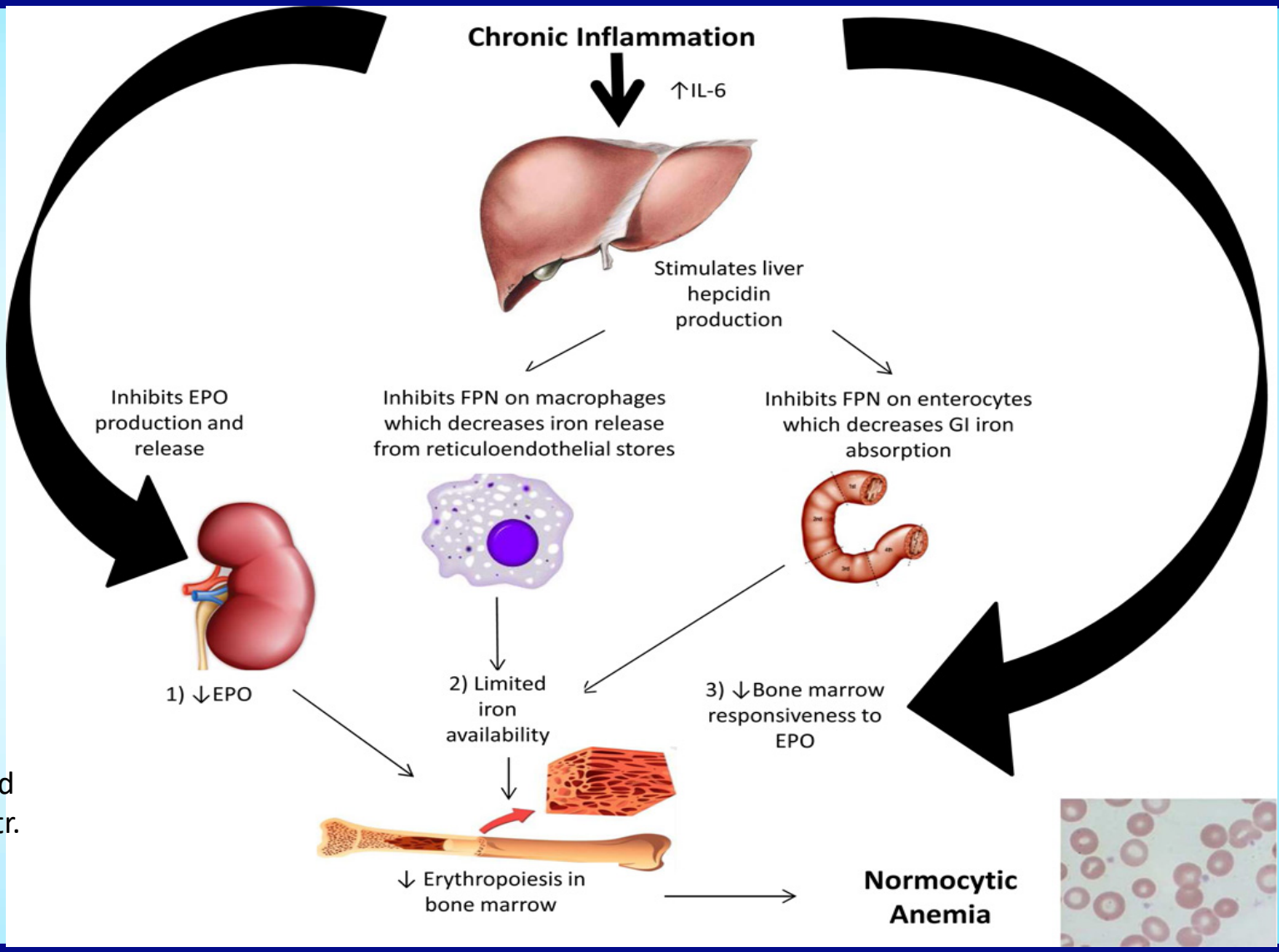
Preziosi P, et al. Double-blind study of a total liver extract in patients with hepatic dysfunction. Int J Clin Pharmacol Biopharm. 1975;11(3):210-5.

Iron Support

Ferrochel iron amino acid chelate - each tablet contains 29mg Fe

- For low iron labs
  - Total iron
  - Hg/HCT/RBC/RDW
  - Total iron binding capacity
- % saturation
- Iron metabolism altered in chronic metaflammation
- Metaflammation = cornerstone of metabolic signaling issues

Osterholm EA, et al. Chronic inflammation and iron metabolism. J Pediatr. 2015;166(6):1351-57.



Osterholm EA, et al. Chronic inflammation and iron metabolism. J Pediatr. 2015;166(6):1351-57.

Iron Support

- Also use AMLA PE 50% (powdered extract)
- *Phyllanthus emblica* – AKA Indian gooseberry
  - Ayurvedic herb very high in vitamin C
  - Also effective in reducing hypercholesterolemia

Usharani P, et al. BMC Complement Altern Med. 2019;19:97.

AMLA

- Randomized, double-blind placebo-controlled study 2019
- 98 dyslipidemic patients – Amla or placebo
- RESULTS:
  - 39% reduction in atherogenic index in plasma (AIP)
  - Significant reduction in TC, LDL-C and TG levels
  - Also ratio of apoB/apo A-I improved (reduced)
  - No alteration in CoQ10 levels
  - Trends in FBS lowering
  - Dose: 1 tablet 1-3 times a day

Upadya H, et al. BMC Complement Altern Med. 2019;19:27.

Metal and Pesticide Detoxification

- Intestinal binders good for metals
  - Activated charcoal
  - Sodium alginate
  - Bentonite clay
  - Chlorella
  - Acacia gum
  - Aloe vera leaf

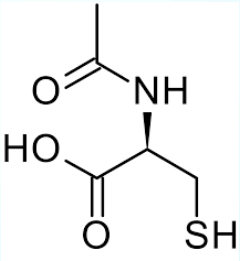
Metal and Pesticide Detoxification

- Cilantro (Coriandrum sativum)
  - Antioxidant
  - Reported to detoxify mercury, lead
  - Decreases lead absorption into bone
  - Also inhibition of delta-aminolevulinic acid dehydratase (ALAD) enzyme

Abascal K, Yarnell E. Cilantro-culinary herb or miracle medicinal plant? *Alternative and Complementary Therapies*. 2012;18:259–264.

Metal and Pesticide Detoxification

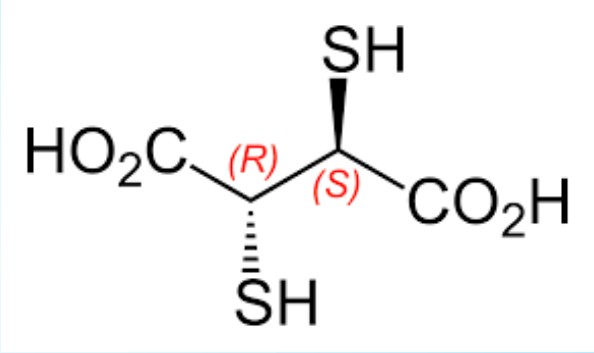
- ALA 600mg QD
  - Antioxidant
  - Regenerates other antioxidants – Vit E, C, reduced glutathione
  - Metal chelating ability
  - Fat and water soluble
- NAC – n-acetylcysteine 750mg BID
  - Antioxidant
  - Oral precursor of cysteine
  - Chelates toxic elements
  - Stimulates glutathione synthesis



- Celery seed oil – improves kidney detox; phthalate detox
- Fulvic acid – pH balance; detoxifies pesticides, contaminants

Sears ME. Chelation: harnessing and enhancing heavy metal detoxification – a review. Scientific World J. 2013;2-13:219840.

DMSA - Dimercaptosuccinic acid



- Supports the body's natural detoxification abilities
- Most effective oral mercury chelator
- Also effective for lead, arsenic, cadmium
- Chelates mercury in the blood, liver, kidneys and eliminate toxic deposits from the brain
- 100mg orally or suppository

Frumkin H, et al. Diagnostic chelation challenge with DMSA: a biomarker of long-term mercury exposure? Environ Health Perspect. 2001;109(2):167-71.

Protein Support

- VEGAN protein blend
- Supports protein levels
- Supports weight loss and performance
- 22 mg / serving RICE and PEA

protein

- Superior Digestibility
- Mix 2 scoops in 8 ounces beverage ; drink

daily in AM

What is Homeopathic Drainage

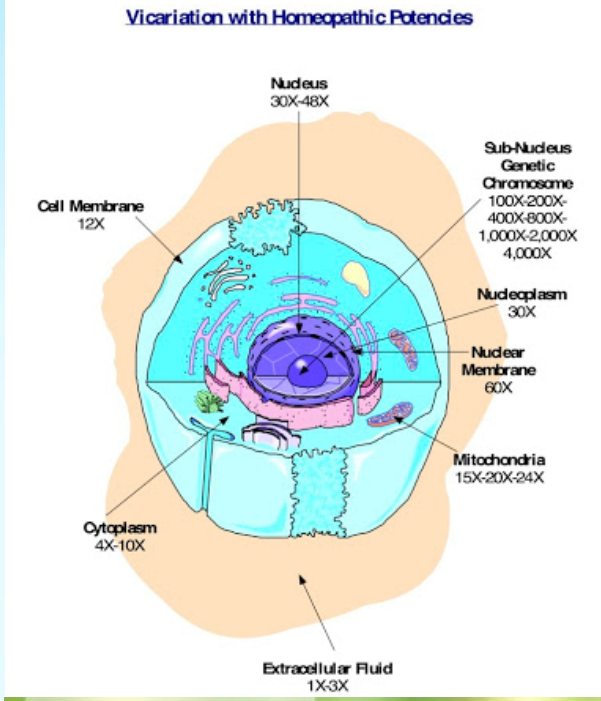
- Use of homeopathic medicines to facilitate detoxification/repair detoxification processes
- More than just herbals
- Targets specific tissues systems and supports cell signaling
- Makes detoxification more efficient and tolerable

Drainage Targets

- Lymph
- Liver
- Kidney
- Lung
- Skin
- Colon

Homotoxicology: Mitochondrial Resuscitation and Endocrine Targeting

- Aging: Tissues can no longer utilize energy for repair/cannot overcome endocrine inefficiency in signaling response.
- Target endocrine structures to rejuvenate hormone receptor signaling



Ernest E, et al. Homotoxicology: a review of randomized clinical trials. Eur J Clin Pharmacol. 2004;60(5):299-306.

Drainage Lymph Primary Remedies

- Phytolacca
- Conium
- Thuja
- Scrophularia
- Calcerea Carbonica