# The Liver

Health & Support of the "Chief Metabolic Organ"

Karen Falbo, CN

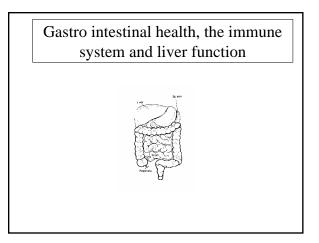
# Liver Functions

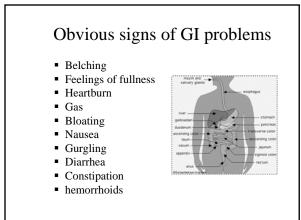
- Storing energy in the form of sugar (glucose)
- Storing vitamins, iron, and other minerals
- Making proteins, including blood clotting factors, to keep the body healthy and help it grow
- Processing worn out red blood cells
- Making bile which is needed for food digestion
- Metabolizing or breaking down many medications and alcohol
- Killing germs that enter the body through the intestine

# The liver has as many as 500 vital functions

- The livers diverse functions connect the digestive system to every other system in the body
  - The immune system
  - Endocrine system
  - Nervous system
  - Cardiovascular system
     this hard-working organ requires 30% of the cardiac output to perform i
- Overall all metabolic-cellular-functions depend on the liver.

[]] Arias IM, Jakoby WB, Popper H, Schacter D, Shafritz DA: The Liver: Biology and Pathobiology, 2nd Edition NewYork: Raven Press, 1988.

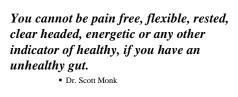




# Unobvious

- Joint and muscle pain
- Headaches (food intolerance, gall bladder and liver
- stress)

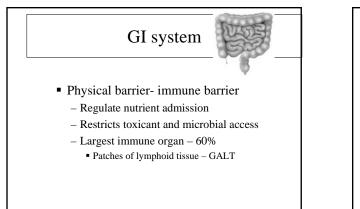
  Heart palpitations (food allergies, nutrient deficiencies,
- etc.)
- Mood swings
- Skin rashes, acne
- Nose bleeds
- Weak fingernails (low minerals and low HCI)
- Coated tongue
- Frequent illness
- Allergies
- Fatigue

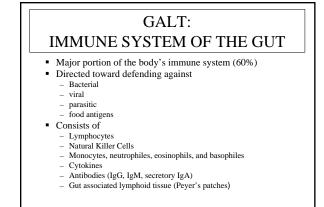


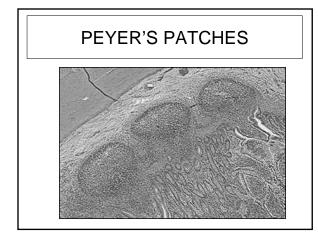


# The physical immune barriers

- Skin
- Mucous membranes of the mouth, genitals, nose, and eyes
- the lung lining
- and the whole intestinal system
- Injury of any kind or even a change in cellular structure of the membrane can allow invasion







# PEYER'S PATCHES

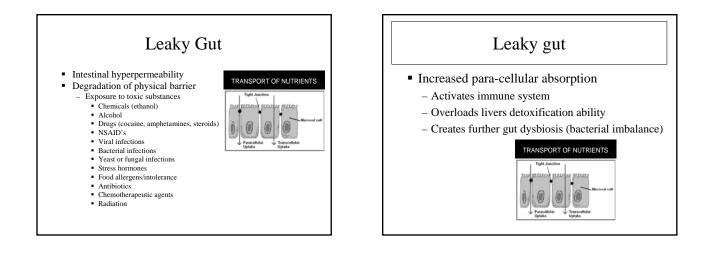
- Consists of lymphoid follicles that release lymphocytes after antigen processing
- These lymphocytes migrate to the mesenteric lymph nodes, the systemic circulation and back to specific mucosal sites where they provide protective immunity from the offending antigen.

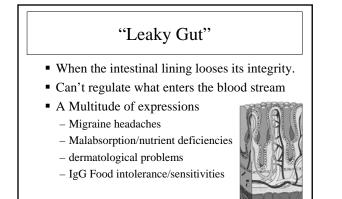
## Damage to the mucosal lining

- From infection (bacterial, viral, fungal)
   Dysbiosis (unhealthy bacteria produce mixed acid waste which damage the mucosal lining)
- From food intolerance (gluten, casein, etc.)
- From antibiotics, chlorine, food additives, etc.
- From chemicals (drugs (prescription and recreational), alcohol, ethanol, antibiotics, etc.)
- From nutrient insufficiency (vitamin A, GLA, amino acids, etc.)

## Toxins leak into the blood stream

• Any crossing of the barrier by what is considered foreign by the immune system will result in activation of the system and the defense forces will rally.



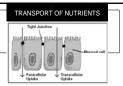


# A multitude of expressions

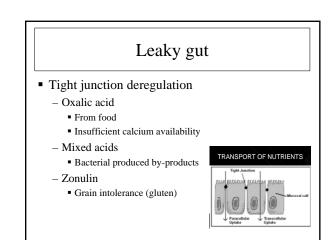
- Fatigue
- Muscle and joint pain
- Neurological and/or cognitive problems
- Mood disorders
- Bowel problems
- Urticaria (chronic hives)
- <u>Autoimmune disease</u>
- And more.....



# Leaky Gut



- Tight junction regulation
  - Calcium
    - Calcium uses para-cellular transport to travel from the gut to the blood where it binds. Once bound, the tight junctions close.
  - Cytokines
    - Cells of the immune system come from the blood side through the tight junctions to clean up certain antigens in the gut.



# Zonulin

- A study a number of years ago found that the proteins from wheat and corn could induce a leaky gut in rats which had first been made niacin deficient.
- Since then, other work has found that there is a relationship between exposure to the wheat protein gliadin and the excess production of a talented disrupter of the tight junction called zonulin.
- Zonulin's presence (similar to lack of calcium) opens up the tight junctions between cells.
- Scientists found that zonulin was elevated both in serum and in the lumen of the gut in celiac disease.
- They also learned by monitoring people with skin reactions to gluten called dermatitis herpetiformis, that this leaky gut/zonulin phenomenon was a part of the disease process that occurred before the flattening of the villi.
- They learned that the disruption caused by zonulin could be set in motion by a simple exposure to gliadin.

# CD and non-celiac-gluten-intolerance is Genetic

- Research in human genes
  - **non-**celiac gluten sensitivity
    - immune reactions to gluten
    - affect as many as 81% of the American population

According to Kenneth Fine, M.D., director of the Intestinal Health Institute in Dallas, Texas.

# Gene Testing

- Human leukocyte antigens or HLA
- several types of HLA genes within each person
- It is a particular type called HLA-DQ that is most useful to identify gluten sensitivity
- Assessment of the probability that a person may be gluten intolerant,
  - If a person possess the celiac genes further testing is necessary to diagnose the disease.
  - If a person possess non-celiac-gluten-intolerant genes they should treat themselves like a celiac.
- EnteroLab 972-686-6869 or https://www.enterolab.com

# Identifying Leaky Gut Lactulose/mannitol test

- Lactulose and mannitol
  - water-soluble substances
  - not metabolized by the body
  - are excreted intact in the urine
- Lactulose
  - a large disaccharide
  - made of galactose and fructose
  - normally not well absorbed and should not be present in large amounts in the urine
- Mannitol
- a monosaccharide
- a monosaccharide
   normally well absorbed
- is present in greater amounts in the urine

# Lactulose/mannitol test

- After an overnight fast, a pre-test urine specimen is provided.
- Then the person drinks a solution containing lactulose and mannitol.
- Urine is then collected for the following six hours and tested.
- If mannitol levels in the urine are low, then absorption of smaller molecules may be compromised due to a digestive problem other than LGS.
- If lactulose levels are high it is indicative of increased permeability to large, potentially antigenic molecules.17
- Miller, A. The pathogenesis, clinical implications and treatment of intestinal hyperpermeability. 1997;2:330-345

# Healing Leaky gut

- *Remove* the substances causing intestinal inflammation and LGS.
- *Replace* the impaired digestive mechanisms with digestive aids.
- *Reinoculate* the bowel with friendly flora and correct dysbiosis.
- *Repair* the mucosal lining of the intestinal tract with foods and supplements.

# **Remove** the substances causing intestinal inflammation

- A food allergy elimination/challenge diet
   rest the digestive system and the immune system
- Dirty Dozen Elimination/Challenge
   Dairy products, wheat (and other gluten-containing grains), eggs (whites particularly), corn, peanuts, tomatoes, shellfish, citrus fruits and juices, sugar, chocolate, coffee, soy, artificial sweeteners, and yeast.
- Removal of caffeine, alcohol, problematic prescription drugs (seek qualified doctor or practitioner), and junk foods is necessary as well.

# **Food Allergy Testing**

#### Serum IgG

- delayed sensitivity (2-3 days)
- Evidence of integrity of physical barrier
   Leaky gut
- Leaky gut
   Requires rotation diet
- Requires rotation u
- Serum IgE
  - Immediate reaction (runny nose, itchy eyes, etc.
  - Complete elimination
- Skin scratch histamine

## On an elimination diet, what is left to eat? Abundant choices!

- Fish, chicken, turkey, buffalo, lamb, lean beef, pork
- Beans and legumes (black beans, pinto beans, etc.)
- Whole grains (brown rice, quinoa, millet, etc.)
- Fruit (berries, peaches, pears, plums, apples, kiwi's, etc.)
- Vegetables (cruciferous, leafy greens, carrots, cucumber,
- sweet potatoes, squash, etc.)
- Almonds, pecans, pine nuts, macadamia nuts, etc.Coconut milk, almond milk, hazelnut milk
- Ghee, coconut oil, olive oil, etc.
- Fresh herbs, spices, garlic, sea salt, etc.

## Remove pathogenic microorganisms Functional assessment of GI health

- Comprehensive Digestive Stool Analysis along with other tests offered by Genova Labs, www.gdx.net, 1-800-522-4762
- Important information about the ecology of the GI tract
  - intestinal wall integrity
  - small bowel bacterial overgrowth
  - yeast presence
  - immune function
  - parasite activity
  - specific intolerances
  - Helicobacter infection

# Anti-fungal, anti-bacterial, antiparasitic support

#### Garlic

 potent anti-fungal properties, G.S. Moore and R.D. Atkins, "The fungicidal and fungistatic effects of an acueous garlic extract on medically important yeast-like fungi, Mycologia 69 (1977): 341-Oregano oil

- oregano is over 100 times more potent than caprylic acid against Candida J.C. Stile et al. "The inhibition of Candida albicaus by oregano" / Applied Nutr 47 (1995): 96-102 Virastop or Candidase enzyme formulas (protease and cellulase enzymes)
  - Bacteria and parasites are made of proteins
  - viruses have protein coatings or 'films,' and yeasts have
  - outer shells consisting of cellulose and protein Proteases and cellulases can help break these intruders down, and then carry off the toxins and dead cells the destroyed
  - pathogens leave behind.
  - http://www.enzymestuff.com/conditionleakygut.htm#4

## Anti-fungal, anti-bacterial, anti-parasitic support

- Citrus Seed Extract
- Olive leaf extract
- Berberine: This alkaloid is found in various plants, including goldenseal, barberry, and Oregon grape. Berberine exhibits a broad spectrum of antibiotic activity, including activity against bacteria, protozoa, and Candida fungi. Y. Kaneda et al., "In vitro effects of berberine sulfate on the growth of entamoeba histolytica giardia lamblia, and trichomonas vaginalis," Annals Trop Med Parasitol 85 (1991): 417-25.

## Replacing

- Digestive enzymes (plant or microbial)
- Taking a digestive enzyme facilitates digestion and lessens the antigenic load.
- Enzymes break down the food particles so they do not exist as larger particles that will physically irritate the gut lining or activate the immune system.
- Remember that if gastritis or ulcer is present, avoid HCL.

#### Brush border enzymes Substrate Enzymes Product Alpha-dextrinase alpha-dextrins glucose Glucomylase (Maltase) Maltose glucose Sucrase-Isomaltase Sucrose glucose & fructose Lactase Lactose glucose & galactose Trypsin Enterokinase Trypsinogen Peptidases Terminal amino

acids

Nucleotides

Aminopeptidase
Dipeptidase Nucleosidases

& Phosphtases

Peptides & amino acids Nitrogenous bases

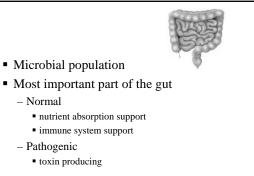
pentoses

# SMALL INTESTINE VILLI: **BRUSH BORDER**

## Reinoculate

Friendly flora

- Lactobacillus and Bifidobacter
  - · decrease gut pH which prevents the growth of harmful organisms · compete for nutrients and attachment sites with potentially
  - pathogenic organisms
  - produce antimicrobial factors and promote proper IgA secretion for immunity 29,3
- Especially after antibiotic use
- The bifidobacteria have been shown to restore microflora balance in extremely compromised adults and to improve bowel function.34



# Feed the good bacteria

- Drinking green tea helps
  - inhibits the growth of harmful organisms, such as Clostridium species and promotes the growth of beneficial Lactobacillus and Bifidobacter species.
- Foods high in FOS feed and promote the growth of Bifidobacter species.
  - honey, onion, burdock, rye, asparagus, Jeruselum artichoke, banana and oats (gluten-free available at Vitamin Cottage).

Yamamoto T, Juneja LR, Chu D, Kim M. <u>Chemistry and applications of green tea</u>. Boca Raton, FL: CRC Press; 1997

# Repairing

#### Dietary Fiber create

- Short-Chain Fatty Acids (SCFA) butyrate, acetate and propionate
- primary fuel for the colon
- derived from fermentation of soluble fiber by colonic bacteria
- Soluble fiber also decreases the pH of the intestines, encouraging the growth of beneficial organisms and suppressing the growth of unfriendly organisms.25

# **L-Glutamine:**

Principal fuel used by the cells of the small intestine for growth and repair. Circulating and tissue levels of glutamine drop drastically after infection injury or trauma.

- Is needed for glutathione formation. Glutathione is vital for liver detoxification which is compromised in LGS.
- Glutamine also increases the height of the villi and the thickness of the
- mucosa. Secretory IgA is promoted by glutamine.
- The presence of secretory IgA strengthens the intestinal barrier and diminishes bacterial adherence and translocation to other parts of the body.
- Lastly, glutamine is needed for glucosamine synthesis which is essential for the synthesis of mucin, the protective mucous layer in the gut.

Miller, A. The pathogenesis, clinical implications and treatment of intestinal hyperpermeability. 1997;2:330-345 Souba WW. <u>Glutamine: physiology, biochemistry and nutrition in critical illness</u>. Austin TX: RG Landes Co.; 1992.

# **Fish Oil**

- Omega-3, EPA/DHA
- Modulates inflammation
  - decreases the production of inflammatory hormones, leukotriene B4, thromboxane A2, tumor necrosis factor, and pro-inflammatory 2series prostaglandins
  - increases the formation of less inflammatory 3series prostaglandins and thromboxanes

Miller, A. The pathogenesis, clinical implications and treatment of intestinal hyperpermeability. 1997;2:330-345 Belluzzi A, Brignola C, Campieri M, et al. Effect of an enteric-coated fish oil preparation on relapses in Crohn's *J Med* 1996;334:1557-1560

# Antioxidants

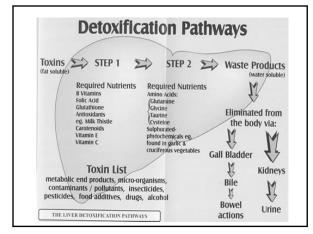
- Antioxidants such as vitamin C, vitamin E, selenium, carotenes and zinc
  - help protect against free-radical damage to intestinal cells
  - Support glutathione production (a primary nutrient required for liver detoxification)
  - Help protect against intermediates produced through phase I liver detoxification

## Detoxification

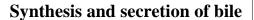
- The liver is the central organ of detoxification
- The body eliminates toxins either by directly neutralizing them or by excreting them in the urine, feces, lunges, and skin.
- Toxins that the body is unable to eliminate build up in the tissues, typically in fat storage.

- Toxins are produced
  - endogenously
  - exogenously
- Primary endogenous toxins
  - Normal metabolic processes
  - Hormones
  - Leftover histamines from allergic reactions
  - Released by pathogenic organism infection

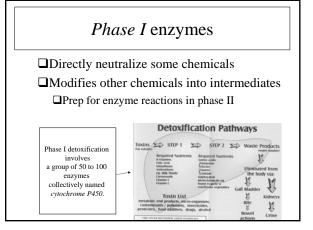
- Primary exogenous toxins
  - Pesticides and chemicals in food and water
  - Chemicals (house-hold cleaning products, skin and body-care products, plastics, off-gassing of building materials (carpet, plywood, flooring, etc.), environmental contaminants, etc.)
  - Air pollution
  - Artificial food additives
  - Nicotine, alcohol, caffeine
  - Drugs (prescription and recreational)
  - Etc.



- The level and type of internally produced toxins increase greatly when metabolic processes go awry, typically as a result of nutritional deficiencies.
- Murray, Michael N.D. & Pizzorno, Joseph N.D., 1998. Encyclopedia of Natural Medicine 2nd Ed. Prima Pub.



- Bile a carrier in which many toxic substances are effectively eliminated from the body.
- The toxin-carrying bile is sent to the intestine were it may be absorbed by fiber and excreted.
- Low fiber diets result in poor bonding with the feces and reabsorption of the toxins.
   Supplement with soluble fiber
  - Supplement with solub
  - Apples
    Guar gum
  - PsylliumPectin
  - Pectin
    Citrus fruits
- Furthermore, bacteria in the intestines often modify these toxins so that they become even more damaging.



# Cytochromes P450 categories

• Groups

- family I
- sub-type A2
- Each enzyme works best in detoxifying certain types of chemicals, but with overlap in activity.
- They all metabolize the same chemicals, but with differing levels of efficiency.

# Activity of the various cytochrome P450 enzymes varies

- From one person to another
  - Genetics
  - Level of toxin exposure
  - Nutritional status
    - Macro-nutrient dependant (protein, carbohydrate, fat)
    - Micro-nutrient dependant (vitamins, minerals, amino acids, fatty acids, co-factors)

# **Bio-transformation**

- When cytochrome P450 metabolizes a toxin, the result is a chemically transformed-substance
  - made water-soluble (less toxic)
    - e.g. Neutralizing caffeine
  - or converted to a more chemically active form (more toxic intermediate)
    - Ready for phase II

# Intermediates are often more chemically active, thus more toxic

- Each toxin metabolized by Phase I, generates a free radical
- If the Phase II detoxification system is not functioning adequately, these intermediates hang around and are far more damaging.

# Free-radical quenching

- Without adequate free-radical defenses, every time the liver neutralizes a toxin, it is damaged
- Glutathione the most important antioxidant for neutralizing the free radical/intermediates
   Is also required for more of the key Phase II detoxification processes
- Glutathione gets used up by free radicals from Phase I
  - Depletion halts Phase II which is glutathione dependent
- Murray, Michael N.D. & Pizzorno, Joseph N.D., 1998. Encyclopedia of Natural Medicine 2nd Ed. Prima Pub.

# Daily nutrients intake required for Glutathione production • Selenium 200 mcg. • Riboflavin 50-200 mg. • N-acetyl-cysteine (NAC) 300 – 600 mg. • alpha-lipoic acid 100 - 300 mg. • vitamin C 1,000 mg. • vitamin E 400 IU's • L-cysteine and L-glycine (check with a practitioner) • Supplemental glycine has been particularly associated with aiding in times of increased detoxification demand. • A deficiency of any of these nutrients may adversely impact glutathione-associated detoxification capacity<sub>µ</sub>

[i] New Perspective in Nutritional Therapies. HealthComm Conference packet. 1996

# Functional Assessment –

### Genova diagnostic Laboratory

- A comprehensive profile of Liver Detoxification
- Assesses the body's capacity to carry out detoxification
- Common substances are used through these functional challenges-caffeine, acetaminophen, and salicylate-
  - evaluates specific aspects of the detoxification process and free radical damage
  - The rate of caffeine clearance in either saliva or plasma parallels the activity of the cytochrome P450 enzymes.
- Measuring oxidative damage
  - impaired liver function can lead to higher levels of free radicals (which have been linked to further liver damage.)

# Additional Nutrient Support

#### SAMe (S-Adenosylmethionine)

- involved in over 40 biochemical reactions in the body
- SAMe works by contributing to methylation reactions the process of adding a carbon-hydrogens unit (a methyl group) to another molecule.
- Methylation reactions are critical for many body functions and in the manufacturing of many body components,
  - brain chemicals
  - detoxification reactions
  - and production of joint components
- Additionally, methylation protects our DNA -- the building blocks of all cells -- from damage.

# SAMe

#### a central player in liver biochemistry

- Half of all methionine in the body is used in the liver to make SAMe
- Two of its crucial functions in the liver are methylation and the production of glutathione.
- SAMe performs two other functions in the liver:
   it helps in liver regeneration
  - and bile flow, or "sluggish liver."
- The liver actually has special SAMe enzymes just for regenerating tissue.
- In terms of "sluggish liver," one of the leading contributors to impaired liver function is diminished bile flow or cholestasis,
- Symptoms may including

   PMS, chemical sensitivities, fatigue, digestive disturbances, allergies and constipation.

# Milk thistle

- contains flavonoids called silymarin
  - exert a substantial effect on protecting the liver from damage as well as enhancing detoxification processes.
  - Silymarin prevents damage to the liver by acting as an antioxidant, increasing the synthesis of glutathione, and by increasing the rate of liver tissue regeneration.
- •

 Hikino K, Kiso Y. Antihepatotoxic actions of flavonolignans from Silybum marianum fruits. *Planta Medica*. 1984; 50:248-250.

# Phosphatidylcholine (PC)

- derived from lecithin
- composed of a phosphate group, 2 fatty acids, and choline
  - choline is required for the proper metabolism of fats (lipotropic effect), export of fat from the liver
  - acts in the human body as a methyl donor (liver detoxification, brain health/mood, joint health)
  - In the absence of adequate choline, fats become trapped in the liver, where they block metabolism.
  - Stagnation of fat and bile eventually leads to the development of more serious liver disorders such as cirrhosis.

# Choline has recently been designated as an essential nutrient.

#### Best food sources

- As free choline, organic vegetables (especially cauliflower and lettuce), whole grains, organic-liver, and non-GMO-soy.
- As lecithin (containing 10-20% phosphatidylcholine), in grains, legumes, organic-meat and egg yolks.

#### Deficiency symptoms

- Liver and kidney disorders develop when animals are fed a choline-deficient diet.
- Fatty infiltration of the liver and other signs of liver dysfunction develops in humans fed a choline-deficient diet.

Canty, DJ and Zeisel, SH. Nutr Reviews. 52;327-339, 1994; Zeisel, SH, et al. FASEB J 5;2093-2098, 1991

# Phosphatidylcholine: treatment for a variety of liver disorders

- Cirrhosis of the liver
- Decreased bile solubility
- Diabetic fatty liver
- Acute & Chronic Viral Hepatitis: Numerous controlled trials have established PC as a safe and potent intervention for infection (Mueing 1972, Hinyama 1980, Yamol 198, Iosina 1981, Joshins 1982, Visco 1985, Hantak 1990, Ilic and Begic-Janev 1991). Optimal results were achieved in these studies when subjects were maintained on a combination of oral and infused PC utilizing higher doses. Once clinical indicators began returning to normal subjects were maintained on oral doses of PC. In addition to decreases in liver enzymes, serum lipids, immune markers and bilirubin, subjects experienced reversal of fatty degeneration, inflammation, jaundice, liver swelling and fibrosis, per liver biopsy.

# Cleansing diet

- **Upon arising**: high-fiber supplementation and 1 8ounce glass of filtered water with fresh lemon juice
- Before breakfast: 1 cup dandelion root tea and or 1 cup green tea and probiotic supplement and L-glutamine (wait 30 minutes for breakfast)
- Breakfast: 1 apple; 2 soft-boiled or hard-boiled eggs; steamed fresh kale, and red bell peppers with dash of thyme take multiple vitamin/mineral supplement, digestive enzyme, fish oil supplement, additional antioxidant supplements, calcium/magnesium 2:1

# Cleansing diet

- **Midmorning**: 2 eight-ounce glasses of filtered water and ½ c. berries
- Lunch: 4 ounces broiled lamb chop with rosemary; cleansing salad (watercress, tomatoes, radish, and sprouts); dressing of olive oil, fresh lemon, and chives. Take a digestive enzyme with meal, B-complex, vitamin C and fish oil supplement.
- **Midafternoon**: 2 eight-ounce glasses of water, miso broth or vegetable broth
- **4 P.M**. 1 <sup>1</sup>/<sub>2</sub> cups organic strawberries or other berries or 8 oz. of vegetable juice

# Cleansing diet

- **Dinner**: 4 oz. poached fresh salmon with dill; salad bowl (minced parsley, chopped tomatoes, and diced scallions with olive oil, lime juice, and mint); steamed Brussels sprouts; 1 cup dandelion tea
- Midevening: high-fiber supplementation and 2 eight-ounce glasses of filtered water
- Before Bed: Take milk thistle