



## NATUROPATHIC WISDOM NOTES

428 Quadra Ave, Campbell River, BC. V9W 6T9 Tel: 250-286-3655 or 800-898-6699 Fax: 250-850-2078  
Email: doctor@drpincott.com Web: www.DrPincott.com Hours: Tue-Fri 9:00 AM – 6 PM. (After hours pickup available.)

*It is really hard to tell the difference between good luck and bad luck.*

Pat Skinner

### Liver Health or Functional Hepatology

There are two stories of male patients ending up with liver transplants because of the damage caused by the livers inability to detoxify common everyday substances taken in combination. This is due to the genetic individuality that affects function. For instance the drug Cimetidine taken at the same time as an exposure to environmental toxins such as insecticides can disrupt detoxification pathways in the liver so much so that it can lead to liver failure and ultimately liver transplant in susceptible individuals.

The same story may happen with those susceptible individuals who say have the flu and are taking acetaminophen for treatment, drink a glass of wine everyday, are sleep deprived and eat a poor quality diet. This individual sued the drug company because there was no warning on the label that acetaminophen could contribute to liver failure when combined with alcohol. Now on all bottles of acetaminophen you will now find a warning that taking it along with alcohol can cause liver death.

In the US 3 Billion dollars are spent annually on liver diseases such as hepatitis B, C, biliary cirrhosis, cirrhosis and infections of the gallbladder with no known cause or origin.

The liver is a **metabolic, immune and endocrine organ** and controls the relationship of immune defence, eliminating endogenous and exogenous toxins, handles metabolic recycling of nutrients such as glucose, fatty acids and amino acids and their nitrogen metabolites that need to be detoxified. Nitrogen atoms in amino acids are uniquely difficult to eliminate from the body and require a specialized detoxification pathway in the liver called the urea cycle. Nitrogen is excreted as a neutral pH molecule called urea which is two molecules of ammonia stuck together. Other animals eliminate nitrogen as ammonia. Bacterial putrefaction can produce nitrogenous wastes such as putrecine and cadaverine (the cause of odorous bowel movements) that can modify distant tissues such as the central nervous system. This means that you can get a headache or irritability from a toxic bowel!

The liver is important for **fat, carbohydrate and protein metabolism**. It is the major organ for **cholesterol synthesis** itself through the HMG CoA reductase pathway that is blocked by statin drugs. The liver synthesizes plasma protein such as **albumin** which transports other substances such as hormones to distant tissues and **apolipoproteins** which are water soluble and transport lipids throughout the body. The liver, by way of the bile, **emulsifies fats** in the digestive tract to make them into micellized forms that are water soluble and more easily taken up by the cells as metabolic fuel. Bile is composed of three ingredients: cholesterol, bile salts and lecithin (phospholipid). The liver synthesizes bile acid from cholesterol as a way to excrete cholesterol from the body. This reaction is activated by vitamin C and magnesium. If the blood cholesterol level is elevated this may be due to the backup of cholesterol excretion due to a low bile acid level resulting in light colored stools, fat malabsorption. Inflammation of the gallbladder results and so does an increase risk of heart disease due to elevated cholesterol. Heart disease and gallbladder disease is therefore very much interrelated so by improving bile acid synthesis not only is the gallbladder and fat

digestion improved but the risk to heart disease is also lowered.

**Carbohydrate metabolism** is controlled the liver and can produce elevated lipids and triglycerides associated with sugar intolerance if the wrong types are consumed and in excess. Sugar that is "time released", or complex carbohydrate, is metabolized over hours rather than a "quick release" sugar or simple carbohydrate which is metabolized in minutes affecting blood fat metabolism very differently.

**Hemoglobin metabolism** is associated with liver function and is measured by bilirubin in the blood, which is a breakdown product of hemoglobin. The liver is associated with building things up, anabolism, (proteins, triglycerides, phospholipids and glycogen) as well as breaking things down, catabolism, (detoxification processes as well as reducing proteins, fats and carbohydrates into smaller molecules like carbon dioxide, water and energy) and it does both these processes at the same time.

### Causes of Liver Distress

The liver is a very dynamic organ with a huge ability to regenerate itself. It can hypertrophy or can be smaller in size if it is not overworked. 10% of the liver is made up of kupffer cells which are the white cells of the liver responsible for the immunological function of the liver. They take its message by way of the hepato-portal blood and the gastrointestinal mucosal system where 60% of the immune system of the body resides in the gut associated lymphoid tissue (GALT). These activated tissues of the gut send messages to the liver kupffer cells stimulating inflammatory mediators that affect the liver locally and the body systemically thus the liver is an immune organ and has an inflammatory capability. Visceral adipose tissue, that fat that secretes directly into the portal blood directly to the liver, stimulates the formation of **adipokines** or reactive inflammatory molecules.

The immunological function of the kupffer cells is improved by: lowering the load of **proinflammatory molecules** such as food allergens, antigens, xenobiotics (hormone mimicking toxins in our food and environment), heavy metals, antigens and improving liver antioxidant defense and detoxification. Chronic diseases of fatigue, chronic muscle pain, sleep disturbances, restlessness and low energy syndrome are related to slight overburdens of the livers detoxifying and regenerative abilities and that although the serum liver function tests are within "normal range" the actual functional ability of the liver is compromised.

Dr. Sies, the father of the term "**oxidative stress**", first studied these oxidative reactions using liver tissues because the liver is so actively engaged in oxygenase enzyme activities which combine oxygen with various molecules to cause tissues to release oxidants that have the potential to damage adjacent tissues when not properly regulated or controlled. Upregulated liver cell function then stresses the mitochondria of the cells that further releases free radicals causing liver damage. Using anti-oxidant therapies this process can be controlled.

The pressure on the liver by the environment is composed of four categories: drugs (pharmaceuticals as well as recreational),

alcohol, nutrition and by products of gut metabolism ( the enteric bacteria) which release their own by-products that the liver needs to metabolize.

**The liver has a lot of things going on simultaneously and it may be this interrelationship between the livers functional reserve and the liver stress factors that tips the balance towards the increasing prevalence we see in chronic liver diseases of unknown origin.**

**Detoxification** of the **phase 1** (cytochrome P450 enzymes) and **phase 11** systems of the liver very much depend on the genetic variations of the individual as per the two stories above making some people yellow canaries. The first pass of detoxification can vary by 1000 fold between individuals and explains the yellow canary effect of environmentally sensitive individuals who react to low exposures of toxins. Some substances can alter the rate of detoxification of the phase 1 altering the effect of drugs ie grapefruit, 300cc of grapefruit juice per day, lowers the rate of detoxification of phase 1 and keeps the drug in the body's system longer and is often used in transplant patients so that their drugs are retained longer (ie cyclosporin), but it can also get in the way of detoxifying other substances and drugs that need to be detoxified. Cruciferous vegetables enhance phase 11 detoxification pathways to balance out the altered phase 1 detoxification so therefore the diet can be selected individually.

There are tests that can be done to measure not only the genotype test ie **slow metabolizer** or **fast metabolizer** but also the phase I and phase II imbalances (contact our office for more information). Alcohol affects detox pathways such that in the alcoholic individual, , the P450 system is overtaxed creating oxidized intermediates that need to be detoxified by phase 11 conjugation with glutathione. This then uses up their stores of glutathione rapidly resulting in accumulation of these toxic metabolites as they have no where to go. Then they end up with hepatic induced neurologic illnesses as **delerium tremens** and the treatment of choice is **N-acetyl cysteine**, (NAC) which attempts to trap these free radical oxidants and block oxidative injury or cirrhosis of the liver. Other antioxidants as well as glutathione itself can be used to promote this antioxidant function of the liver. **Nutrition interfaces with liver function and the barrier protection it gives against the toxic endogenous and exogenous environment.**

Most hepatitis patients have suffered a severe **emotional stress** in the months before developing the disease. High cortisol levels, secreted during stress, cause immunosuppression and hepatitis C viruses that might have been dormant can become active. A poor diet that is void of fruits and vegetables along with smoking, drinking alcohol and exposure to hepatotoxic solvents in their work or home all interfere with their immunity. If hepatitis C positive patients have a good lifestyle, don't drink or smoke and have a good diet, they are healthy, well into their 70's and 80's and don't even know that they have liver disease. Those who have lots of stress and poor lifestyles get very sick with liver disease.

#### **Evaluation of Liver Function:**

There are six liver enzymes to evaluate on a standard blood test: bilirubin, AST, ALT, GGT, LDH and alkaline phosphatase. These are measured along with albumin, protine and platelets. Naturopathic values for healthy liver function differ greatly from the "normal values" of MD's. (See my website for a sample lab report).

**Treatment:** What can enhance the functions of the liver?

**Four R program:** The four R program does take the load off the liver: remove, , replace, reinoculate and repair. **Remove** refers to the elimination of any pathogenic microflora or parasites that might be present in the gut. **Replace** refers to the replacement of digestive factors or enzymes that might be limited or inadequate. **Reinoculate** refers to the reintroduction of desirable digestive microflora called probiotics to obtain a more desirable balance. **Repair** refers to providing nutritional support for regeneration or healing of the gastrointestinal mucosa.

**Metabolic detoxification** using an elemental (hypoallergenic) diet along with detoxifying herbs enhances phase 1 and phase 11 function of the liver. (Ask about **Dr. Pincott's 2 week detoxification program** that is recommended 1-3 times per year).

**Diet:** Eat 6 servings of green vegetables per day and drink 8 glasses of purified water per day.

**Alpha-lipoic acid** can lower liver enzymes in a matter of weeks and regenerates liver cells thus preventing liver transplants in some patients. It is a very effective mitochondrial stimulant (recycles glutathione) not only for **acute liver disease** but **chronic liver disease** including hepatitis B and C, primary biliary cirrhosis and autoimmune hepatitis. It is the rate-limiting factor for the production of energy by the mitochondria and is produced in plenty when young and healthy. As a person ages and gets sicker the lipoic acid production decreases because the B1, B3 and biotin are depleted as well so be sure and take a good **B complex** for the liver. **Vitamin B6** is very important part of the liver protein metabolic pathway, **B1** is important for proper metabolism of carbohydrates. **Selenium** prevents most viruses from replicating including keeping the hepatitis C virus in check. The herb, **milk thistle**, protects the liver cells from further oxidative damage. Morphine and alcohol enhances hepatitis C replication but this oxidative stress can be controlled by **alpha-lipoic acid, selenium, NAC, milk thistle** and **glutathione**.

**Other nutrients to include:** Make sure you are taking vitamin E, vitamin C, omega 3 essential fats, (Carlson's Cod Liver Oil), psillium husk fiber, probiotics, natural carotenes and a good multivitamin.

**Avoid:** over the counter medications, recreational drugs, smoking, volatile hydrocarbon solvents, general anesthesia if possible, acetaminophen, white flour, white sugar and alcohol, processed foods, foods that contain mycotoxins (aflatoxins as found in peanuts), salty foods and foods high in iron (especially in the presence of liver disease).

Dr. Pincott is proud to announce that October 1, 2005 marks her 20<sup>th</sup> year of practice.

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