It is only the liver that can purify the blood stream and we only have one liver.

**The Liver Detoxification Pathways**

Inside the liver cells there are sophisticated mechanisms that have evolved over millions of years to break down toxic substances. Every drug, artificial chemical, pesticide and hormone, is broken down (metabolized) by enzyme pathways inside the liver cells. Many of the toxic chemicals that enter the body are fat-soluble, which means they dissolve only in fatty or oily solutions and not in water. This makes them difficult for the body to excrete. Fat soluble chemicals have a high affinity for fat tissues and cell membranes, which are made of fatty substances. In these fatty parts of the body, toxins may be stored for years, being released during times of exercise, stress or fasting. During the release of these toxins, symptoms such as headaches, poor memory, stomach pain, nausea, fatigue, dizziness and palpitations may occur.

The body's primary defense against metabolic poisoning is carried out by the liver. The liver has two mechanisms designed to convert fat-soluble chemicals into water soluble chemicals so that they may then be easily excreted from the body via watery fluids such as bile and urine.

**How the Liver Detoxifies Harmful Substances**

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Basically there are TWO major detoxification pathways inside the liver cells, which are called the Phase 1 and Phase 2 detoxification pathways.

**Toxin list:** metabolic end products, micro organisms, contaminants/pollutants, insecticides, pesticides, food additives, drugs, alcohol.

**Phase One - Detoxification Pathway**

An example of the phase one pathway is the Cytochrome P-450 mixed function oxidase enzyme pathway. These enzymes reside on the membrane system of the liver cells (called Hepatocytes).

Human liver cells possess the genetic code for many isoenzymes of P-450 whose synthesis can be induced upon exposure to specific chemicals. This provides a mechanism of protection from a wide variety of toxic chemicals.

To put it simply, this pathway converts a toxic chemical into a less harmful chemical. This is achieved by various chemical reactions (such as oxidation, reduction and hydrolysis), and during this process free radicals are produced which, if excessive, can damage the liver cells. Antioxidants (such as vitamin C and E and natural carotenoids) reduce the damage caused by these free radicals. If antioxidants are lacking and toxin exposure is high, toxic chemicals become far more dangerous. Some may be converted from relatively harmless substances into potentially carcinogenic substances.

Excessive amounts of toxic chemicals such as pesticides can disrupt the P-450 enzyme system by causing over activity or what is called 'induction' of this pathway. This will result in high levels of damaging free radicals being produced.

Substances that may cause overactivity (or induction) of the P-450 enzymes:
- Caffeine, Alcohol, Dioxin, Saturated fats, Organophosphorus pesticides, Paint fumes, Sulfonamides, Exhaust fumes, Barbiturates

The family of P-450 enzyme systems is quite diverse, with specific enzyme systems being inducible by particular drugs, toxins or metabolites. It is this characteristic that has allowed the development of special tests to check the function of the various pathways - see liver tests (SEE BELOW). The substrate is the substance that is acted upon by the enzyme.

Substrates of cytochrome P-450 enzymes:
- Theophylline, caffeine, phenacetin, acetaminophen, Lidocaine, erythromycin, cyclosporin, ketoconazole, testosterone, estradiol, cortisone, Alprenolol, bopindolol, carvedilol, metoprolol, propranolol, Amitriptyline, clomipramine, desipramine, nortriptyline, Codeine, dextromethorphan, ethylmorphine, 4-methoxyamphetamine Family Phenytoin, ibuprofen, naproxen, oxicam drugs, S-warfarin, Diazepam, hexobarbitone, imipramine, omeprazole, alcohol, chlorozoxazone, enflurane.
Phase Two - Detoxification Pathway

This is called the conjugation pathway, whereby the liver cells add another substance (eg. cysteine, glycine or a sulphur molecule) to a toxic chemical or drug, to render it less harmful. This makes the toxin or drug water-soluble, so it can then be excreted from the body via watery fluids such as bile or urine.

Major Phase II pathways include glutathione, sulfate, glycine, and glucuronide conjugations. Individual xenobiotics and metabolites usually follow one or two distinct pathways. Again, this makes testing of the various pathways possible by challenging with known substances.

The conjugation molecules are acted upon by specific enzymes to catalyse the reaction step. Through conjugation, the liver is able to turn drugs, hormones and various toxins into excretable substances. For efficient phase two detoxification, the liver cells require sulphur-containing amino acids such as taurine and cysteine. The nutrients glycine, glutamine, choline and inositol are also required for efficient phase two detoxification. Eggs and cruciferous vegetables (eg. broccoli, cabbage, Brussels sprouts, cauliflower), and raw garlic, onions, leeks and shallots are all good sources of natural sulphur compounds to enhance phase two detoxification. Thus, these foods can be considered to have a cleansing action. The phase two enzyme systems include both UDP-glucuronyl transferase (GT) and glutathione-S-transferase (GSH-T). Glutathione is the most powerful internal antioxidant and liver protector. It can be depleted by large amounts of toxins and/or drugs passing through the liver, as well as starvation or fasting. Phase II reactions may follow Phase I for some molecules or act directly on the toxin or metabolite.

Substrates of the glycine pathway

Salicylates and benzoate are detoxified primarily through glycination. Benzoate is present in many food substances and is widely used as a food preservative. Many other substances are detoxified as well via the glycine conjugation pathway. Patients suffering from xenobiotic overloads and environmental toxicity may not have sufficient amounts of glycine to cope with the amount of toxins they are carrying.

Substrates of the sulfation pathways

Neurotransmitters, steroid hormones, certain drugs such as Acetaminophen (also known as paracetamol) , and many xenobiotic and phenolic compounds.

Substrates of glucuronidation

Polycyclic aromatic hydrocarbons, steroid hormones, some nitrosamines, heterocyclic amines, some fungal toxins, and aromatic amines. It also removes "used" hormones, such as estrogen and T4 (thyroid hormone) that are produced naturally by the body.
Toxic Overload

If the phase one and two detoxification pathways become overloaded, there will be a build up of toxins in the body. Many of these toxins are fat soluble and incorporate themselves into fatty parts of the body where they may stay for years, if not for a lifetime. The brain and the endocrine (hormonal) glands are fatty organs, and are common sites for fat-soluble toxins to accumulate. This may result in symptoms of brain dysfunction and hormonal imbalances, such as infertility, breast pain, menstrual disturbances, adrenal gland exhaustion and early menopause. Many of these chemicals (e.g. pesticides, petrochemicals) are carcinogenic and have been implicated in the rising incidence of many cancers.

Rarely does anyone think about the liver, which seems incredible to me because it is such a powerful organ and is easily improved. Indeed the simplest and most effective way to cleanse the blood stream and thus take the load off the immune system is by improving liver function.

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LIVER REFERENCES: PHASE II


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http://www.CancerHerbal.com
The purpose of this page is to assist people to understand the reasons for the tests that are generally performed and make some sense of the results. It is not intended to encourage "self diagnosis". A reliable diagnosis of a liver condition can only be made by a qualified medical practitioner after many factors have been investigated and ruled out. This will involve taking a full medical history and more than likely more tests will need to be performed. Therefore if it is always recommended to see your physician if you suspect you have a liver problem.

What causes the enzymes to be raised in a Liver Function Test?

The reason why all or some of these enzymes become elevated in cases of liver disease is that they are normally contained inside the liver cells (hepatocytes). They only leak into the bloodstream when the liver cells are damaged. Thus measuring liver enzymes is only able to detect liver damage and does not measure liver function in a sensitive way. "The Healthy Liver and Bowel Book" page 98 - 99.

Other tests can be done to check the ability of the liver to manufacture its vital proteins. These are tests for the proteins albumin, prothrombin, and various globulins and they show characteristic abnormalities in those whose liver function is abnormal. This may sound rather technical, however your doctor can easily do all these tests from two or three small vials of collected blood. In the early stages of liver disease there may be no dramatic symptoms and thus you and your doctor may be totally unaware that there is an underlying problem. Often the early stages of liver disease are found coincidentally on a routine blood test that includes tests for liver function.

What is a Liver Function Test?

Blood samples are analyzed for levels of specific enzymes in the blood stream – there are generally 5 – 6 specific things that are checked. Collectively these tests are called a "Liver Function Test" or LFT. These enzymes are what are referred to as ‘markers’ of disease and dysfunction. This is not to be confused with a ‘Functional Detoxification Profile” which tests the function of the detoxification pathways.

How reliable is this test?

The name "Liver Function Test" is actually quite misleading as this test does not actually measure the ‘function’ of the liver. It is more a marker of the status of the integrity of the liver cell membranes.

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Most of the standard or routine blood tests that your doctor will order to check "liver function" are in reality only able to detect liver disease. These tests are not sensitive enough to accurately reflect liver function.

**It is possible to still have liver disease even though blood tests are normal.** Therefore the LFT alone is not capable of making a proper diagnosis of many liver conditions. No test is completely accurate as it is only an indication of what is happening at the time the test was taken. It is therefore common practice to perform the test again on another occasion, especially if any results are abnormal.

This is why it is important for you to consult a specialist in liver diseases (hepatologist), if you suspect that your liver is unhealthy and yet conventional blood tests remain normal.

Different diseases of the liver will cause differing types of damage and affect liver function tests accordingly. It can be possible to give an idea of which disease may be suspected from a liver function test, but these tests are not the absolute way of diagnosing liver disease. They are helpful, but not the whole story. They are also useful for monitoring someone with liver disease, but are not always accurate.

As the LFT is really only showing the level of enzymes present in the blood stream it is only showing that some damaging is occurring but does not give an indication of the extent. This is where other tests are required to give a more accurate picture of the extent of the damage after the fact that damage is occurring has been established.

### What is checked in a Liver Function Test?

A routine blood test for liver function will be processed by an automated multichannel analyzer, and will check the blood levels of the following :-

**A Typical Liver Function Test**

<table>
<thead>
<tr>
<th>Result</th>
<th>Unit</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>AP (Alk Phos)</td>
<td>U/L</td>
<td>30 to 120</td>
</tr>
<tr>
<td>GGT (Gamma GT)</td>
<td>U/L</td>
<td>5 to 35</td>
</tr>
<tr>
<td>LD Lactate Dehydrogenase</td>
<td>U/L</td>
<td>100-225</td>
</tr>
<tr>
<td>AST (Aspartate aminotransferase)</td>
<td>U/L</td>
<td>5 to 45</td>
</tr>
<tr>
<td>ALT (Alanine aminotransferase)</td>
<td>U/L</td>
<td>5 to 45</td>
</tr>
<tr>
<td>Albumin</td>
<td>g/L</td>
<td>38-55</td>
</tr>
<tr>
<td>Clotting Studies (Prothrombin Time)</td>
<td>Seconds</td>
<td>11 to 13.5</td>
</tr>
<tr>
<td>Total Bilirubin - Normal range is 3 - 18 umol/L</td>
<td>(0.174 - 1.04mg/dL)</td>
<td></td>
</tr>
</tbody>
</table>

After the result is the laboratory reference range and the units in which the result is expressed.
Each laboratory will provide a "reference range" or 'normal values' This is the average reading that is deemed a 'normal' reading for the majority of the population. This will assist the doctor in determining if the patient's results are abnormal.

The normal values for liver function tests will vary between men and women, at different times of the day and will change as you get older. Different laboratories may have slightly differing reference ranges.

**Liver Enzymes**

- **ALT** - *(alanine aminotransferase)* - was previously called SGPT is more specific for liver damage. The ALT is an enzyme that is produced in the liver cells (hepatocytes) therefore it is more specific for liver disease than some of the other enzymes. It is generally increased in situations where there is damage to the liver cell membranes. All types of liver inflammation can cause raised ALT. Liver inflammation can be caused by fatty infiltration (see fatty liver) some drugs/medications, alcohol, liver and bile duct disease.

- **AST** - *(aspartate aminotransferase)* which was previously called SGOT. This is a mitochondrial enzyme that is also present in heart, muscle, kidney and brain therefore it is less specific for liver disease. In many cases of liver inflammation, the ALT and AST activities are elevated roughly in a 1:1 ratio.

- **AP** - *(alkaline phosphatase)* is elevated in many types of liver disease but also in non-liver related diseases. Alkaline phosphatase is an enzyme, or more precisely a family of related enzymes, that is produced in the bile ducts and sinusoidal membranes of the liver but is also present in many other tissues. An elevation in the level of serum alkaline phosphatase is raised in bile duct blockage from any cause. Therefore raised AP in isolation will generally lead a physician to further investigate this area. Conditions such as Primary Biliary Cirrhosis and Sclerosing Cholangitis will generally show a raised AP. Raised levels may also occur in cirrhosis and liver cancer. Alkaline phosphatase is also produced in bone and blood activity can also be increased in some bone disorders.

- **GGT** - *(gamma glutamyl transpeptidase)* is often elevated in those who use alcohol or other liver toxic substances to excess. An enzyme produced in many tissues as well as the liver. Like alkaline phosphatase, it may be elevated in the serum of patients with bile duct diseases. Elevations in serum GGT, especially along with elevations in alkaline phosphatase, suggest bile duct disease. Measurement of GGT is an extremely sensitive test, however, and it may be elevated in virtually any liver disease and even sometimes in normal individuals. GGT is also induced by many drugs, including alcohol, therefore often when the AP is normal a raised GGT can often (but not always) indicate alcohol use. Raised GGT can often be seen in cases of fatty liver and also where the patient consumes large amounts of aspartame (artificial sweetener) in diet drinks for example.

- **Bilirubin** is the major breakdown product that results from the destruction of old red blood cells (as well as some other sources). It is removed from the blood by the liver, chemically modified by a process call conjugation, secreted into the bile, passed into the intestine and to some extent reabsorbed from the intestine. It is basically the pigment that gives faeces its brown colour.
Bilirubin concentrations are elevated in the blood either by increased production, decreased uptake by the liver, decreased conjugation, decreased secretion from the liver or blockage of the bile ducts.

In cases of increased production, decreased liver uptake or decreased conjugation, the unconjugated or so-called indirect bilirubin will be primarily elevated. In cases of decreased secretion from the liver or bile duct obstruction, the conjugated or so-called direct bilirubin will be primarily elevated.

Many different liver diseases, as well as conditions other than liver diseases (e.g., increased production by enhanced red blood cell destruction), can cause the serum bilirubin concentration to be elevated. Most adult acquired liver diseases cause impairment in bilirubin secretion from liver cells that cause the direct bilirubin to be elevated in the blood. In chronic, acquired liver diseases, the serum bilirubin concentration is usually normal until a significant amount of liver damage has occurred and cirrhosis is present. In acute liver disease, the bilirubin is usually increased relative to the severity of the acute process. In bile duct obstruction, or diseases of the bile ducts such as primary biliary cirrhosis or sclerosing cholangitis, the alkaline phosphatase and GGT activities are often elevated along with the direct bilirubin concentration. (See Gilbert's Syndrome)

- **Albumin** - Albumin is the major protein that circulates in the bloodstream. As it is made by the liver and secreted into the blood it is a sensitive marker and a valuable guide to the severity of liver disease.

  Low serum albumin concentrations indicate the liver is not synthesizing the protein and is therefore not functioning properly. The serum albumin concentration is usually normal in chronic liver diseases until cirrhosis and significant liver damage is present. There are many other proteins synthesized by the liver however the albumin is easily, reliably and inexpensively measured.

- **Platelet count** - Platelets are cells that form the primary mechanism in blood clots. They're also the smallest of blood cells. They are derived from the bone marrow from the larger cells known as megakaryocytes. Individuals with liver disease develop a large spleen. As this process occurs, platelets are trapped within the sinusoids (small pathways within the spleen) of the spleen. While the trapping of platelets is a normal function for the spleen, in liver disease it becomes exaggerated because of the enlarged spleen (splenomegaly). Subsequently, the platelet count may become diminished.

- **Prothrombin time (Clotting Studies)** The prothrombin time is tested to evaluate disorders of blood clotting, usually bleeding. It is a broad screening test for many types of bleeding disorders. When the liver is damaged it may fail to produce blood clotting factors.

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How do the liver cell membranes get damaged in the first place?

Inflammation is a common cause of damage to the delicate liver cell membranes. Liver inflammation is medically termed hepatitis (hepato = liver, itis = inflammation). This has many different causes including long term alcohol excess, some medications such as long term antibiotics, cholesterol lowering medications and pain killers, oral synthetic hormone replacement, viral infections of the liver such as hepatitis A, B & C, auto-immune hepatitis.
hemachromatosis, primary biliary cirrhosis, exposure to toxic chemicals such as insecticides & pesticides & organic solvents & incorrect diet.

Fatty liver can cause raised Liver Function Test results

One of the most common causes of liver inflammation is fatty liver (see section on Fatty Liver). Fatty liver is also known as NASH, which stands for Non-Alcoholic Steatorrhoeic Hepatosis. It is very common in overweight persons, over the age of 30 who have had a long term poor diet high in processed foods, sugar, saturated fat and dairy products.

Generally an ultrasound of the abdominal area should also be performed. Many cases of fatty liver can be picked up this way. The ultrasound will detect areas of increased echogenicity meaning that the liver tissue is beginning to become infused with fat.

What can be done to lower the readings?

In my medical practice where I do a lot of routine blood tests for hormone levels and liver function in overweight patients, I often find slight elevations in liver enzymes which signifies mild impairment of liver function and slight liver damage. This can easily be reversed with "The Liver Cleansing Diet" principles and specific dietary supplements. I have found that it is very difficult for many of my overweight patients to lose weight even though they may be eating only normal amounts, unless I first improve their liver function. Once they are five to six weeks into the "Liver Cleansing Diet" their liver-function tests are usually back to normal and the process of weight loss takes on increased momentum. Yes, the liver is the strategic organ for those who have found it very difficult to lose weight or simply just to maintain a healthy weight as they get older.

TESTS FOR LIVER DISEASE

If you suspect that your liver is not working properly or may be diseased, ask your doctor to check your liver. The liver can be seen with various imaging techniques, such as ultrasound scanning or CAT scanning, which are done by a radiologist. An ultrasound scan of the upper abdomen will show the size and shape of the liver, gallbladder, spleen, and pancreas. CAT scanning is used to check for cancer or tumors of the liver.

Blood tests can check levels of serum bilirubin and bile acids, which may be elevated in certain types of liver and gallbladder disease. If the bilirubin is too high you may also notice that your bowel actions are very pale and that your urine is a darker color because bilirubin is diverted from the bowels to the urine.

When diagnosing liver disease, often, but not always the most used test in each disease is generally:
What is a Biopsy?

This procedure involves using a special needle to remove tissue from the liver to be examined in the laboratory. This will be used to assess the extent of scarring, fatty infiltration or liver damage.

For the biopsy, you will lie on a hospital bed on your back or turned slightly to the left side, with your right hand above your head. After marking the outline of your liver and injecting a local anesthetic to numb the area, the physician will make a small incision in your right side near your rib cage, then insert the biopsy needle and retrieve a sample of liver tissue. In some cases, the physician may use an ultrasound image of the liver to help guide the needle to a specific spot.

How accurate is this test?

It is still regarded as the most accurate way of assessing the status of the extent of damage to the liver. You will need to hold very still so that the physician does not nick the lung or gallbladder, which are close to the liver. The physician will ask you to hold your breath for 5 to 10 seconds while he or she puts the needle in your liver. You may feel a dull pain. The entire procedure takes about 20 minutes. Liver biopsy is considered minor surgery and is done at the hospital. However it should be noted that this procedure is not without risk – it is important that it is carried out by a very experienced doctor. The risks include puncture of the lung or gallbladder, infection, bleeding, and pain. The bleeding in particular is a dangerous complication. It carries about a 1/10 000 death rate – some doctors say it's even higher.

Who should NOT have this procedure done?

- People with blood clotting disorders
- People who are on blood thinning medication such as Warfarin, Coumadins, Ibuprofin, aspirin
- People with hemangiomas (benign liver cyst consisting of twisted congested blood vessels)

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What is an ultrasound or sonograph?

This is a non invasive method of assessing liver health. It is an imaging procedure of the internal organs of the abdomen, including the liver, gallbladder, spleen, pancreas and kidneys. The ultrasound machine sends out high-frequency sound waves, which reflect off body structures to create a picture. There is no ionizing radiation exposure with this test. There are many reasons for performing an abdominal ultrasound including looking for a cause of pain, for stones in the gallbladder or kidney, or for a cause for enlargement of an abdominal organ. The reason for the examination will depend on your symptoms.

THE LIVER CLEANSING DIET

The ground breaking concepts in this best selling book made Dr Cabot a household name and opened the eyes of millions around the world to the importance of the liver to maintain a healthy body and immune system. Hundreds of delicious liver cleansing recipes will help you to apply the liver friendly principles to your life. Look good and feel great on The Liver Cleansing Diet.

Dr Cabot's book contains invaluable information for all readers.

- The unique 8 week eating plan to detoxify and control your weight.
- The vital principles of a healthy liver.
- How to help your liver to reverse "fatty liver" and to Improve Liver function for those suffering with hepatitis.
- Steps to overcome child obesity.
- A fascinating insight into the ancient Chinese and naturopathic philosophies on liver problems.
- Liver tonics from herbs and nutritional medicine to speed up weight loss (with scientific references) and to help repair a damaged liver.
- The futuristic artificial liver for those with serious liver disease.

A healthy liver is the key to efficient fat metabolism and weight control.

The liver-cleansing diet has many benefits:

1. Increased energy levels.
2. Detoxification and cleansing of the blood stream.
3. Reduction of inflammation and degenerative diseases.
5. Efficient fat metabolism.
6. Weight control.

The liver is the gateway to the body and takes the load off our precious immune system.

Who Can Benefit

For the thousands of patients who suffer with overburdened immune systems, hepatitis, chronic fatigue, obesity, fatty livers and recurring blocked arteries (even after bypass surgery). Let's not suffer with what I call the "fossilized brain syndrome" where lateral and original thinking becomes a crime.

Remember that a healthy liver will reduce depression and moodiness and therefore enable you to laugh more and not get too overheated or as the Chinese say "gung ho" about life's little tribulations.

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