LABCO
Quality Diagnostics

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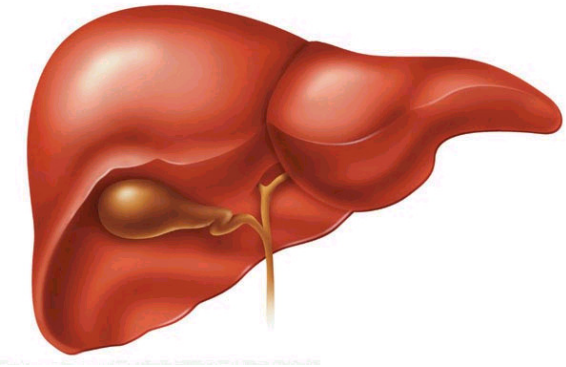
LIVER DETOXIFICATION

The liver plays a key role in most metabolic processes, especially detoxification. The liver neutralizes a wide range of toxic chemicals, both those produced internally and those coming from the environment.
The liver plays several roles in detoxification: it filters the blood to remove large toxins, synthesizes and secretes bile full of cholesterol and other fat-soluble toxins, and enzymatically disassembles unwanted chemicals. This enzymatic process usually occurs in two steps referred to as *phase I* and *phase II*. Phase I either directly neutralizes a toxin, or modifies the toxic chemical to form activated intermediates which are then neutralized by one of more of the several phase II enzyme systems.
Proper functioning of the liver's detoxification systems is especially important for the prevention of cancer. The level of exposure to environmental carcinogens varies widely, as does the efficiency of the detoxification enzymes, particularly phase II. High levels of exposure to carcinogens coupled with slow detoxification enzymes significantly increases susceptibility to cancer.

Phase I Detoxification

The liver's third role in detoxification involves a two-step enzymatic process for the neutralization of unwanted chemical compounds. These not only include drugs, pesticides, and toxins from the gut, but also normal body chemicals such as hormones and inflammatory chemicals (e.g. *histamine*) which become toxic if allowed to build up.
Phase I enzymes directly neutralize some chemicals, but most are converted to *intermediate forms* that are then processed by phase II enzymes. These intermediate forms are much more chemically active and therefore more toxic.



If the phase II detoxification systems are not working adequately, these intermediates can cause substantial damage, including the initiation of carcinogenic processes. People with a very active phase I detoxification system coupled with slow or inactive phase II enzymes are termed *pathological detoxifiers*.
Phase I detoxification of most chemical toxins involves a group of enzymes which, collectively, have been named *cytochrome P450*. Some 50-100 enzymes make up the cytochrome P450 system. Each enzyme works best in detoxifying certain types of chemicals, but with considerable overlap in activity among the enzymes.
The activity of the various cytochrome P450 enzymes varies significantly from one individual to another, based on genetics, the individual's level of exposure to chemical toxins, and his or her nutritional status. Since the activity of cytochrome P450 varies so much, so does an individual's risk for various diseases. This helps to explain why some people can smoke with only modest damage to their lungs, while others develop lung cancer after only a few decades of smoking.

Patients with underactive phase I detoxification will experience caffeine intolerance, intolerance to perfumes and other environmental chemicals, and an increased risk for liver disease, while those with an overactive system will be relatively unaffected by caffeine drinks. One way of objectively determining the activity of phase I is to measure how efficiently a person detoxifies caffeine. Caffeine is an example of a chemical directly neutralized by phase I. Making a toxin water-soluble allows its excretion by the kidneys.
Transforming a toxin to a more chemically reactive form makes it more easily metabolized by the phase II enzymes.

A significant side-effect of phase I detoxification is the production of *free radicals* as the toxins are transformed--for each molecule of toxin metabolized by phase I, one molecule of free radical is generated. Without adequate free radical defenses, every time the liver neutralizes a toxin exposure, it is damaged by the free radicals produced.

The most important antioxidant for neutralizing the free radicals produced in phase I is *glutathione*. In the process of neutralizing free radicals, however, *glutathione* (GSH) is oxidized to *glutathione disulfide* (GSSG). Glutathione is required for one of the key phase II detoxification processes. When high levels of toxin exposure produce so many free radicals from phase I detoxification that the glutathione is depleted, the phase II processes dependent upon glutathione stop.

Phase II Detoxification

Phase II detoxification typically involves conjugation in which various enzymes in the liver attach small chemicals to the toxin.

This conjugation reaction either neutralizes the toxin or makes the toxin more easily excreted through the urine or bile. Phase II enzymes act on some toxins directly, while others must first be activated by the phase I enzymes. There are essentially six phase II detoxification pathways:
· Glutathione conjugation
· Amino acid conjugation
· Methylation
· Sulfation
· Acetylation
· Glucuronidation

Acetaminophen and salicylic acid are a way of objectively determining the activity of phase II.
In order to work, these enzyme systems need nutrients both for their activation and to provide the small molecules they add to the toxins. In addition, they utilize metabolic energy to function and to synthesize some of the small conjugating molecules. Thus, mitochondrial dysfunction, such as found in chronic fatigue syndrome, a magnesium deficiency or physical inactivity, can cause phase II detoxification to slow down, allowing the build-up of toxic intermediates.

REQUIRED SAMPLE:
Phase I:
Saliva after 2h consumption of caffeine *

Phase II:
Urine collection during 10 h (night) after consumption of 650 mg acetaminophen, and 500 mg of salicylic acid. *

***Request sampling procedure for more details.**
TRANSPORT CONDITIONS:
Send chilled and keep frozen.