



hepatic detox profile

The body continually attempts to eliminate chemical toxins through enzymatic processes in the liver. Urinary D-glucuronic acid, a byproduct of phase I detoxification, is a valuable indicator of chemical exposure or liver damage. Urinary mercapturic acids are direct end product metabolites of conjugated xenobiotics. Combined assessment of the urinary levels of the two analytes provides valuable information about exposure to xenobiotics and liver disease, and the capability of the liver to eliminate toxins.

The production, use and disposal of toxic chemicals and synthetic materials have increased the risk of exposure to health threatening toxins. Causal relationships between toxic chemicals and diseases have been well established. However many patients endure chronic symptoms that are associated with exposure to toxins before advanced stages of specific diseases are realized. Thus, there is a great demand for noninvasive laboratory tests that can timely assess chemical exposure and the capability of hepatic detoxification.

One process by which the body eliminates toxins is enzymatic detoxification in the liver. A reliable biomarker for exposure to toxic chemicals is urinary D-glucuronic acid. Elevated levels of D-glucuronic acid indicate induction of cytochrome P-450 enzymes (phase I) as a result of exposure to many xenobiotics

(e.g. pesticides, fungicides, petrochemicals, drugs, toluene, formaldehyde, styrenes, etc.) Such exposures induce the glucuronic acid enzymatic pathway and production of D-glucuronic acid, thus urinary D-glucuronic acid is an indirect by-product of chemical exposure and phase I detoxification reactions.

The urinary level of mercapturic acids indicates quantitatively the degree of activity, or capability of phase II detoxification. Mercapturic acids are the final excretory products of detoxification and include a variety of functionalized xenobiotics that have been conjugated with glutathione or L-cysteine prior to excretion. Low levels of mercapturic acids are consistent with insufficient levels of glutathione and/or cysteine. When the rate of formation of functionalized xenobiotics (phase I) exceeds the capacity of phase II detoxification, more potent toxins accumulate.

Especially important for symptomatic patients or those who have a history of chemical sensitivity, the noninvasive test does not require the use of hepatotoxic compounds. Thorough commentary and treatment recommendations are provided to simplify interpretation. Results are expressed per unit creatinine to normalize for dilution effects, and reference ranges are age and gender specific. It is highly recommended that a concentrated first morning urine specimen is submitted for analysis. The test does not replace comprehensive liver tests for cases of advanced liver disease.

HEPATIC DETOX PROFILE

- **Assessment of status phase I and phase II detoxification**
- **Assessment of chemical exposure and impaired liver function**
- **No hepatotoxic challenge drugs required**
- **Simple first morning void urine collection**

HEPATIC DETOX PROFILE



LAB#: U000000-0000-0
 PATIENT: Sample Patient
 SEX: Female
 AGE: 60

CLIENT#: 12345
 DOCTOR:
 Doctor's Data, Inc.
 3755 Illinois Ave.
 St. Charles, IL 60174

			PHASE I EXPOSURE MARKER				
ANALYTE	RESULT <small>nmole/mg creat</small>	REFERENCE RANGE	PERCENTILE				
			2.5 th	16 th	50 th	84 th	97.5 th
D-Glucaric Acid	130	10 - 200	[Visual representation of percentile distribution for D-Glucaric Acid]				

			PHASE II DETOXIFICATION MARKER				
ANALYTE	RESULT <small>µmole/mmol creat</small>	REFERENCE RANGE	PERCENTILE				
			2.5 th	16 th	50 th	84 th	97.5 th
Mercapturic Acids	84	40 - 95	[Visual representation of percentile distribution for Mercapturic Acids]				

DISCUSSION

The human body attempts to eliminate xenobiotics (foreign organic chemicals) through a concerted effort of enzymatic "functionalization" (phase I) and conjugation (phase II). Functionalization involves chemical modification of the xenobiotic by the cytochrome P-450 or the "mixed function oxidase" enzyme systems. Once functionalized, the altered xenobiotic can then be conjugated and excreted. Urinary D-glucaric acid, a hepatic byproduct of enzymatic response to chemical toxins (phase I), is a reliable indicator of exposure to xenobiotics. Mercapturic acids are direct, excretory end products of the functionalized xenobiotics that have been conjugated with glutathione prior to excretion. Together, the urinary levels of these metabolites provide valuable information about exposure to xenobiotics, liver disease, and quantitative assessment of the status of hepatic phase II detoxification.

D-GLUCARIC ACID MARGINALLY ELEVATED: The level of D-glucaric acid, a marker of exposure to hepatotoxic substances, is marginally elevated for age and gender in this patient's urine sample. This suggests possible mild exposure to xenobiotics with normal detoxification (check mercapturic acids level/phase II activity). Elevated urinary excretion of D-glucaric acid is an indication of induction of cytochrome P-450 enzymes (phase I) in the liver that may be the result of exposure to any of over 200 different xenobiotics (e.g. pesticides, herbicides, fungicides, petrochemicals, drugs, alcohol, toluene, xylene, formaldehyde, styrenes, ibuprofen etc.). Occupational and environmental exposure to toxic compounds causes induction of the glucuronic acid enzyme pathway and production of D-glucaric acid, thus D-glucaric acid excretion is considered an indirect by-product of detoxification reactions. Elevated levels of urinary D-glucaric acid have also been correlated with viral hepatitis and jaundice, and have also been found in patients receiving antirheumatic drugs independent of disease activity. With marginally elevated levels of D-glucaric acid, there may be an increased need for antioxidant protection because toxins that are processed through phase I generate free radicals that require quenching or neutralization. It is important to consider that phase I detoxification tends to become less active with aging.

MERCAPTURIC ACIDS MARGINALLY ELEVATED: The levels of mercapturic acids (MA) in this patient's urine sample are marginally elevated for age and gender, and may be consistent with mild exposure to xenobiotics and enhanced detoxification via glutathione conjugation (phase II). Check for elevated levels of D-glucaric acid as an indicator of xenobiotic exposure. MA are final excretory products of detoxification and include a variety of functionalized xenobiotics that have been conjugated with cysteine, or glutathione. Ideally, urinary levels of MA should be increased with exposure to xenobiotics and enhanced phase I detoxification; MA levels will gradually return to basal levels commensurate with successful hepatic detoxification and removal of the patient from the source of exposure. If warranted, detoxification should be supported with supplemental vitamins C, E, and lipoic acid, selenium, Mg, K, rGSH, and sulfur containing amino acids. It should be noted that falsely elevated levels of MA can occur in patients with cystinuria, or with the use of thiol chelators (D-penicillamine, DMSA and DMPS), and some 'thio-capto' type medications (e.g. thioridazine, captodiamine).

SPECIMEN DATA

Comments:
 Date Collected:
 Date Received: 1/6/2008
 Date Completed: 1/7/2008

Methodology: **Enzymatic**

V05.02