

Hepatic Detox Profile; Urine

TOXIC EXPOSURE MARKERS					
	RESULT	REFERENCE	PERCENTILE		
	per creatinine	INTERVAL	2.5 th	16 th	50 th
			84 th	97.5 th	
D-Glucaric Acid (Phase I)	430 nM/mg	25 - 300	[Visual representation of percentile distribution]		
Mercapturic Acids (Phase II)	67 μM/mM	36 - 90	[Visual representation of percentile distribution]		

URINE CREATININE					
	RESULT	REFERENCE			
	mg/dL	INTERVAL	-2SD	-1SD	MEAN
			+1SD	+2SD	
Creatinine	113	45 - 225	[Visual representation of standard deviation distribution]		

INFORMATION

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 ELEVATED: The level of D-glucaric acid, a marker of exposure to hepatotoxic substances, is abnormally high for age and gender in this sample. The results are consistent with clinically significant exposure to xenobiotics and enhanced phase I detoxification. Check mercapturic acid levels to evaluate the status of phase II detoxification that is required for the final elimination of the toxin(s). Severe xenobiotic exposure with markedly elevated D-glucaric acid levels (>3X normal) may be associated with impaired chemical functionalization or limited 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 been correlated with viral hepatitis and jaundice, and have also been found in patients receiving antirheumatic drugs, independent of disease activity. With elevated levels of D-glucaric acid, there is 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: 11/17/2011	Methodology:
Date Received: 11/21/2011	D-Glucaric: HPLC
Date Completed: 12/5/2011	Mercapturic: Enzymatic