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Pharmacotherapy Handbook, 11e >

## Appendix 6: Drug-Induced Liver Disease

### INTRODUCTION

TABLE A6-1

An Approach to Evaluating a Suspected Hepatotoxic Reaction

Points	-3	-1	0	+1	+2	+3
<b>What is the temporal relationship? (days)</b>						
<i>From the start of therapy</i>	-	-	??	<5	>90	5-90
<i>From the end of therapy</i>	>30	-	??	-	-	<30
<b>Is there evidence of the concurrent use of a hepatotoxin<sup>a</sup></b>	Yes	Maybe	??	-	-	No
<b>Is there an alternate cause, such as, viral hepatitis?</b>	Yes	Most likely—Yes	??	Most likely—No		No
<b>Are there extrahepatic signs or symptoms?</b>						
Dermatologic: rash, palmar erythema, cutaneous vasculitis	-	-	No	Yes (+1 for each)	-	-
Dermatologic: spider nevi, white nails (aka Terry nails)	-	-	No	Yes (+1 for each)	-	-
Hematologic: coagulation disorders	-	-	No	Yes (+1 for each)	-	-
Endocrine disorders: <i>insulin</i> resistance, thyroid dysfunction	-	-	No	Yes (+1 for each)	-	-
Endocrine disorders: adrenal insufficiency, hypogonadism	-	-	No	Yes (+1 for each)	-	-
Skeletal muscular: arthralgias, arthritis	-	-	No	Yes (+1 for each)	-	-
Neurological: encephalopathy	-	-	No	Yes (+1 for each)	-	-
Portopulmonary hypertension	-	-	No	Yes (+1 for each)	-	-
<b>Does the literature support a connection with this drug?</b>						
Listed in the product labeling	-	-	-	-	-	Yes
Published reports in the literature	-	-	-	-	Yes	-
No information available, reaction is undocumented	-	-	Yes	-	-	-
	<b>-3</b>					<b>+4</b>
<b>Results from a rechallenge with the drug.</b>	<b>Negative</b>	-	-	-	-	<b>Positive</b>

<sup>a</sup>drug, herbal remedy, or other occupational exposure known to be potentially hepatotoxic.

A total score of <7 makes it unlikely that this is a hepatotoxic reaction. As the score approaches 14, the possibility that this is a hepatotoxic reaction increases toward certainty. ?? = uncertain.

TABLE A6-2

**Environmental Hepatotoxins and Associated Occupations at Risk for Exposure**

Hepatotoxin	Associated Occupations at Risk for Exposure
Arsenic	Chemical plant, agricultural workers
Carbon tetrachloride	Chemical plant workers, laboratory technicians
Copper	Plumbers, sculpture artists, foundry workers
Dimethylformamide	Chemical plant workers, laboratory technicians
2,4-Dichlorophenoxyacetic acid	Horticulturists
Fluorine	Chemical plant workers, laboratory technicians
Toluene	Chemical plant, agricultural workers, laboratory tech
Trichloroethylene	Printers, dye workers, cleaners, laboratory technicians
Vinyl chloride	Plastics plant workers; also found as a river pollutant

TABLE A6-3

**Relative Patterns of Hepatic Enzyme Elevation versus Type of Hepatic Lesion**

Enzyme	Abbreviations	Necrotic	Cholestatic	Chronic
Alkaline phosphatase	Alk Phos, AP	↑	↑↑↑	↑
5'-Nucleotidase	5-NC, 5NC	↑	↑↑↑	↑
γ-Glutamyltransferase	GGT, GGTP	↑	↑↑↑	↑↑
Aspartate aminotransferase	AST, SGOT	↑↑↑	↑	↑↑
Alanine aminotransferase	ALT, SGPT	↑↑↑	↑	↑↑
Lactate dehydrogenase	LDH	↑↑↑	↑	↑

(See e/Chapter 55, Drug-Induced Liver Disease, authored by William R. Kirchain and Rondall E. Allen, for a more detailed discussion of this topic.)