

Advances in the Diagnosis and Treatment of Acetaminophen Toxicity

LAURA P JAMES, MD

ASSOCIATE VICE CHANCELLOR, CLINICAL AND TRANSLATIONAL RESEARCH
UNIVERSITY OF ARKANSAS FOR MEDICAL SCIENCES

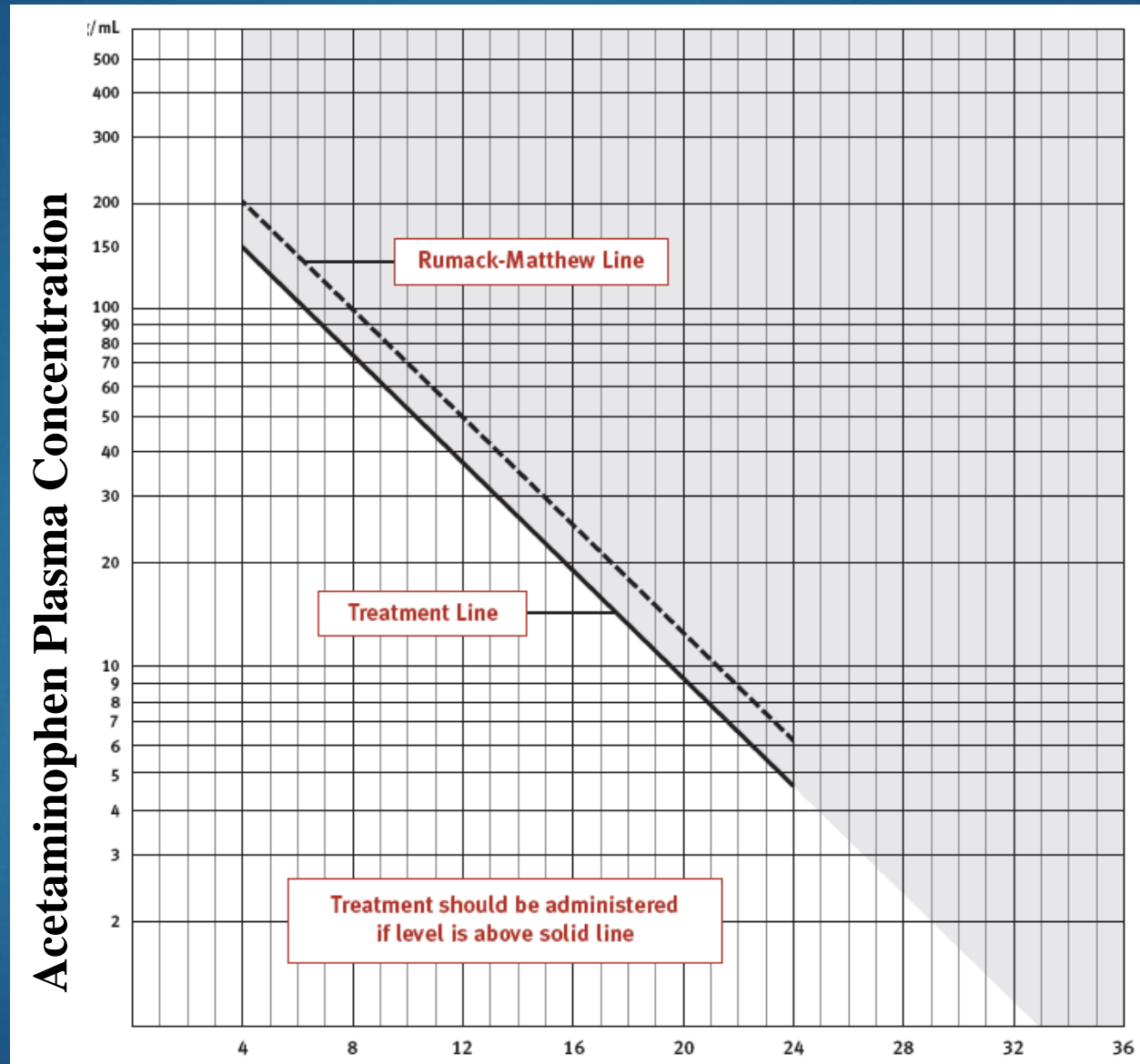
Disclosures

- ▶ Dr. James is the recipient of a STTR grant to develop a new assay for the diagnosis of acetaminophen liver injury (DK079387).

Current approach: diagnosis acetaminophen toxicity

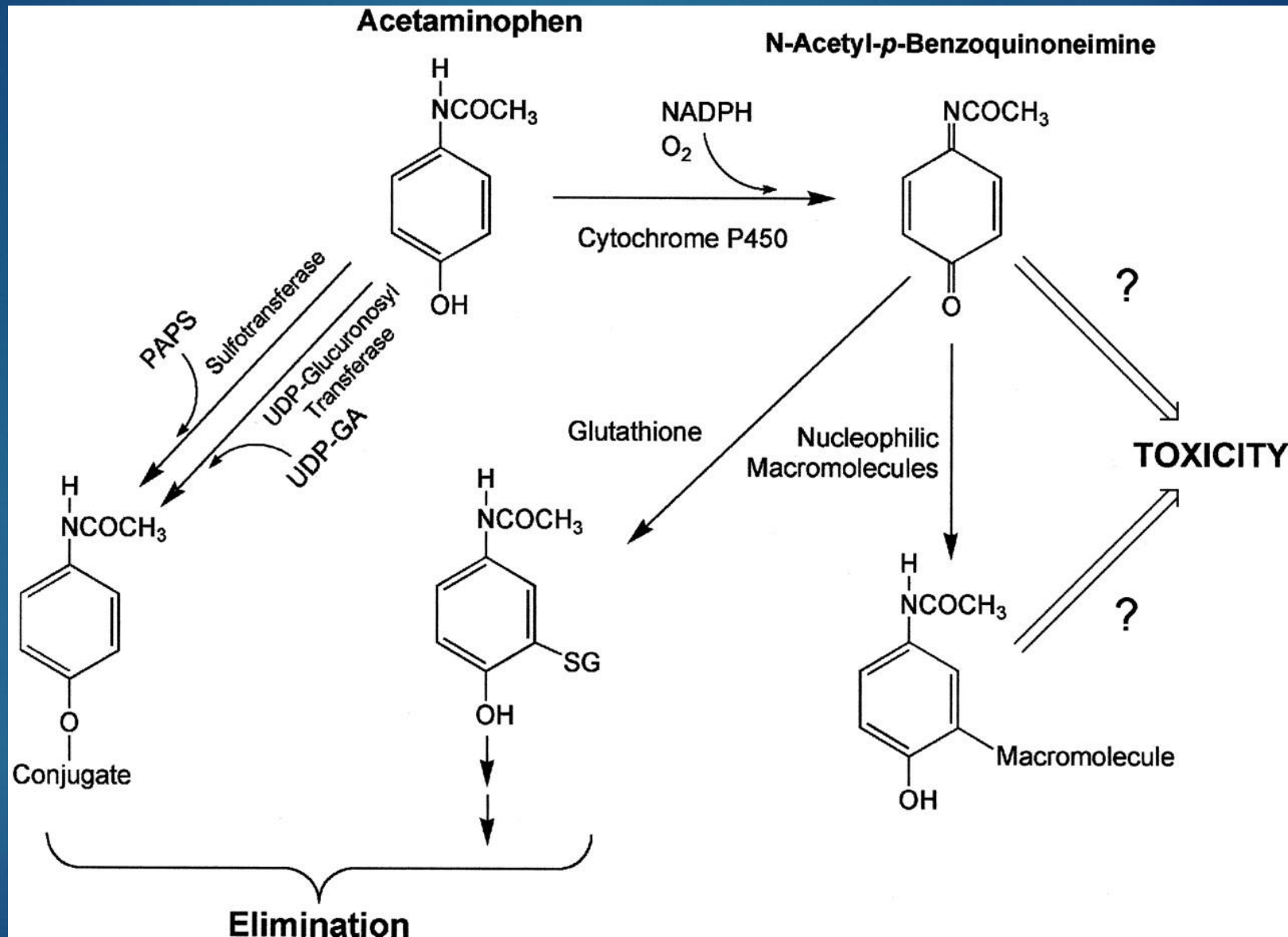
- ▶ Grounded in the Rumack Nomogram
- ▶ Elevation of APAP versus time lapsed since ingestion
- ▶ Widely used for single, acute ingestions
- ▶ Limitations
- ▶ Does not predict who will develop liver injury
- ▶ Limited to initial 24 hours following overdose
- ▶ Does not address disease-drug interactions
- ▶ Dependent on accurate history

Rumack Nomogram - 1976

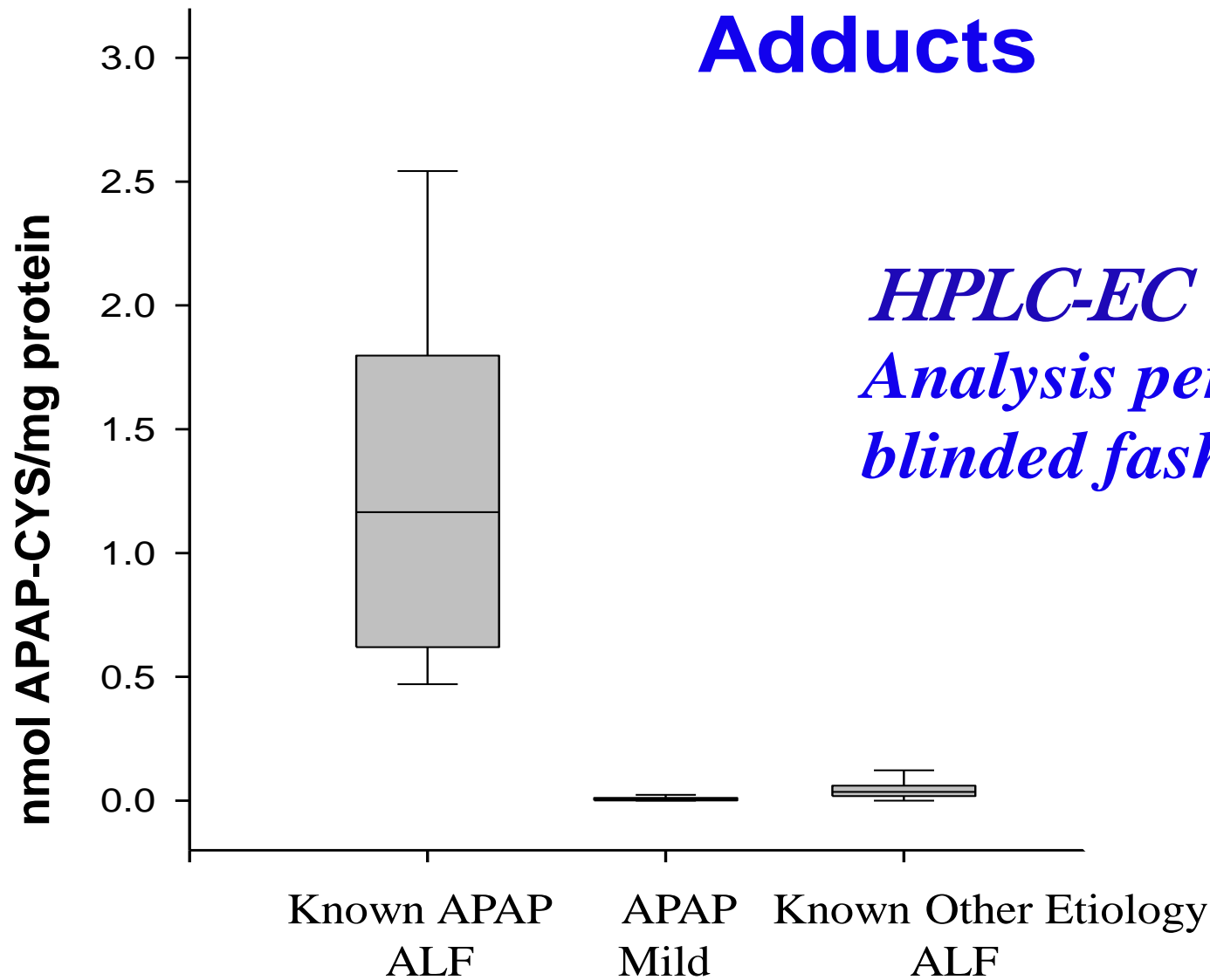


Hours post ingestion

Role of metabolism in acetaminophen toxicity

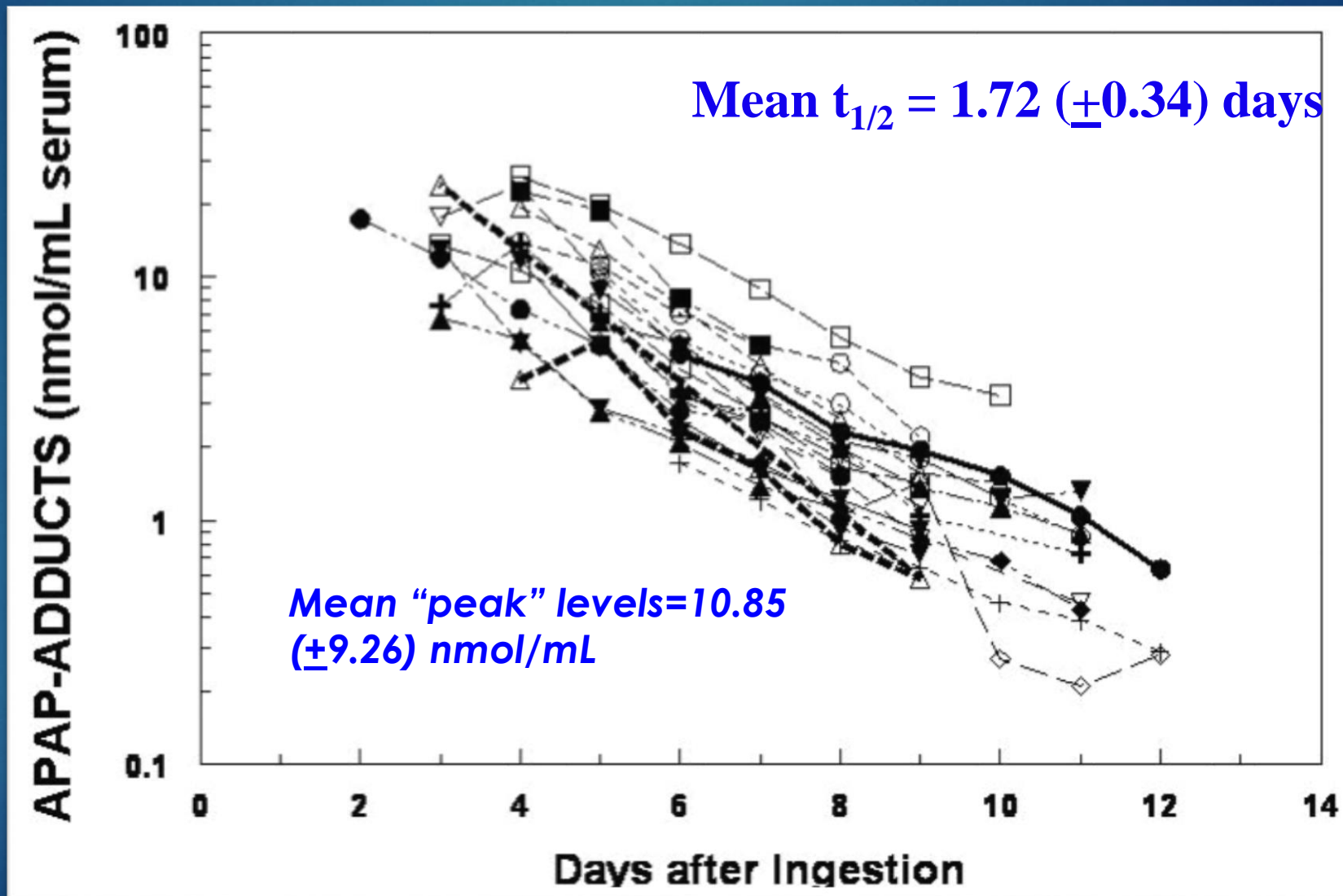


Acetaminophen-Protein Adducts



HPLC-EC
Analysis performed in
blinded fashion

Elimination Profile: Adults with Acute Liver Failure

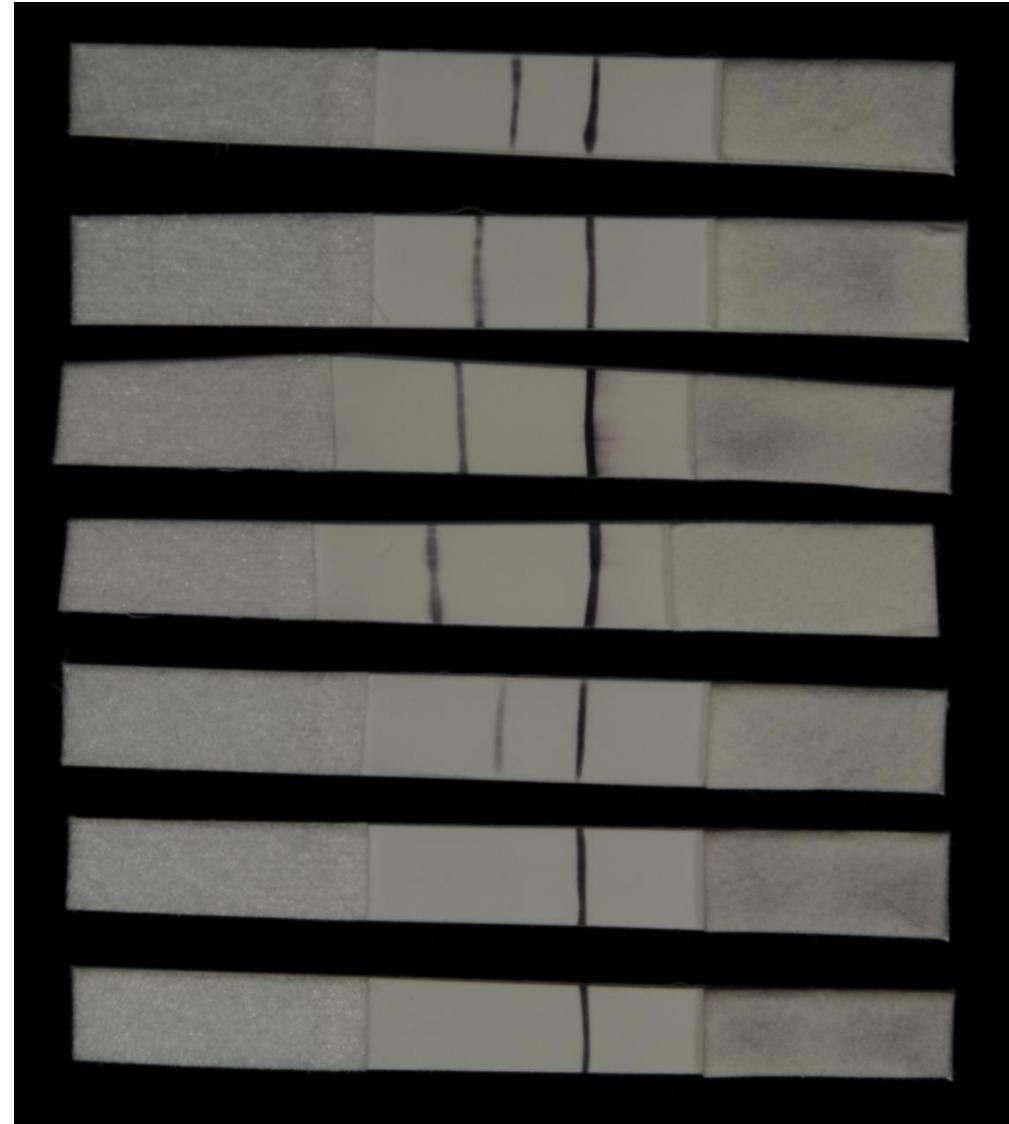


Lateral flow assay

Prototype

TB CB

Description	HPLC-EC Adduct (nmol/mL)
Control, no anti-adduct antibody	----
Control - Antibody, no sample	----
Control – no Acetaminophen exposure	0
Therapeutic Dose Acetaminophen	0.018
Mild Acetaminophen Overdose	0.23
Toxic Acetaminophen Overdose	7.08
Toxic Acetaminophen Overdose	13.04



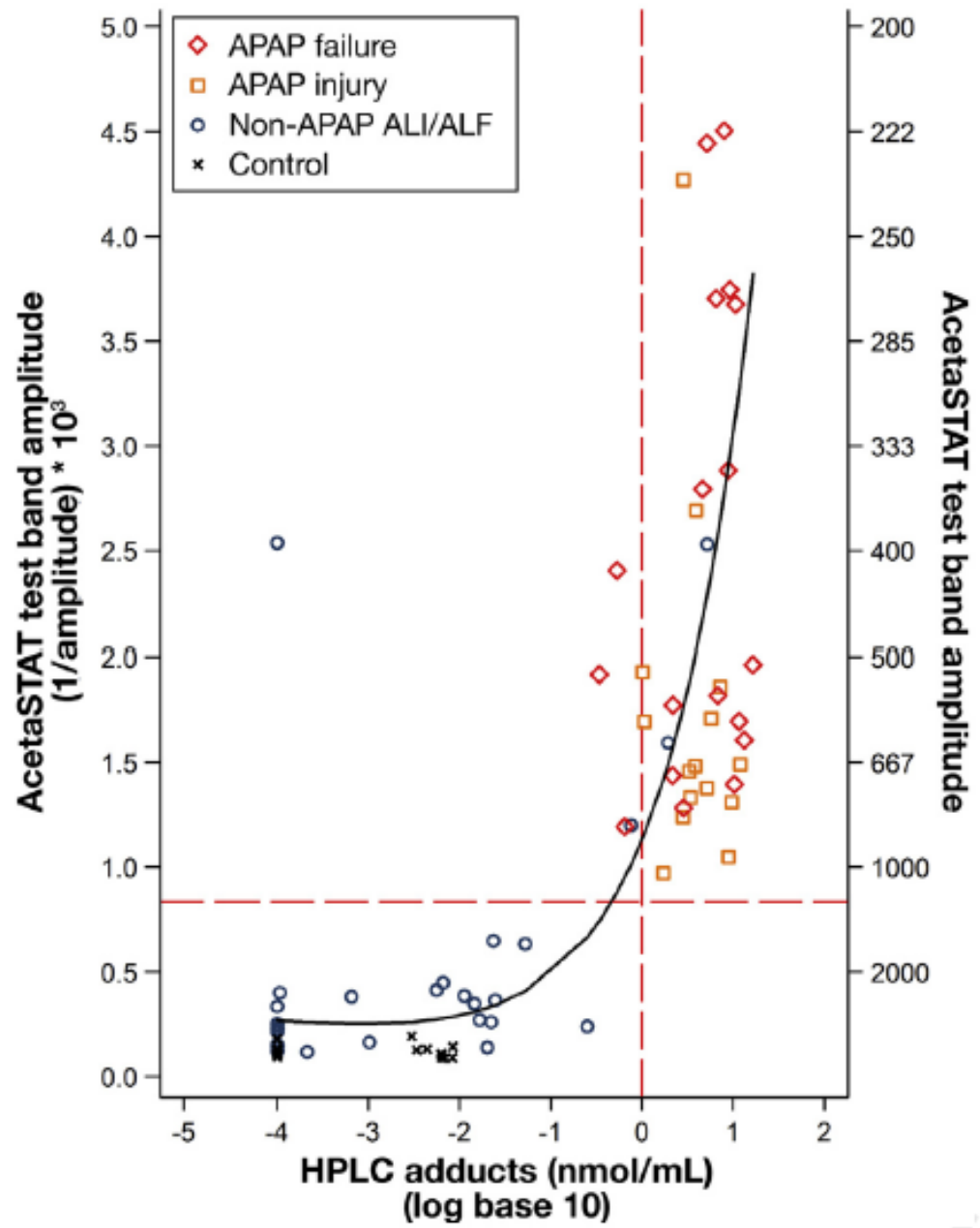
PANCREAS, BILIARY TRACT, AND LIVER

An Immunoassay to Rapidly Measure Acetaminophen Protein Adducts Accurately Identifies Patients With Acute Liver Injury or Failure



Dean W. Roberts,^{*,‡,§} William M. Lee,^{||} Jack A. Hinson,^{*,‡} Shasha Bai,^{*,§}
Christopher J. Swearingen,^{*,§} R. Todd Stravitz,[¶] Adrian Reuben,[#] Lynda Letzig,^{*,§}
Pippa M. Simpson,^{**} Jody Rule,^{||} Robert J. Fontana,^{‡‡} Daniel Ganger,^{§§} K. Rajender Reddy,^{|||}
Iris Liou,^{¶¶} Oren Fix,^{##} and Laura P. James^{*,‡,§}

	ALFSG Study Group			p value
	Controls (19)	APAP (33)	Non-APAP (29)	
Study day ALT (IU/L)	19 (10-48)	3652 (549-8870)	1124 (16-7730)	<0.001
→ AcetaSTAT® Amplitude	8971 (5151-11,108)	584 (222-1027)	3678 (394-8289)	<0.001
→ HPLC-EC (nmol/mL)	0 (0-0)	5.2 (0.3-16.6)	0 (0-5.2)	<0.001
Study day Bilirubin (mg/dL)	0 (0-0)	3.5 (0.6-38.9)	10.2 (0.8, 38.8)	<0.007



Treatment

- ▶ N-acetylcysteine – oral 72 hour protocol
- ▶ Acetadote (IV) – 21 hour protocol.
- ▶ Extension of treatment in patients with persistent toxicity.
- ▶ Indicated in suspected acetaminophen overdose/liver injury.
- ▶ No RCT's; observational data, small studies.