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Measuring AST, ALT and Other Enzyme Activities in Serum

(A look back; 63 years later)

Arthur Karmen, M.D.

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As a second-year medical student at NYU in 1952, I was interested in finding a research project to work on. A cardiologist, Dr. Felix Wroblewski, suggested that I might search for a blood marker for acute myocardial infarction, thinking that damage to the heart muscle might release intracellular enzymes into the circulation. With a \$200 grant, I started in summer 1952 to work on finding a suitable method to measure products of serum glutamic oxalacetic transaminase (SGOT; now AST) Using a paper chromatography method that took 3-4 days to do, I presented results in the spring of 1953.



Serum Enzymes come from Tissues:

- Biochemists AE Braunstein, PP Cohen, and J Awapara had found and measured enzymes in cells of heart, liver, skeletal muscle, kidney, and others;
- these tissue are rich in transaminases, also called aminophosphatases, and more recently aminotransferases;
- when tissues are injured (hypoxia, chemicals, or other processes), their intracellular enzymes may be released into the circulation;
- could blood activity of the enzymes be used to measure or assess damage to the tissue?



The enzymes were first named for the products produced:

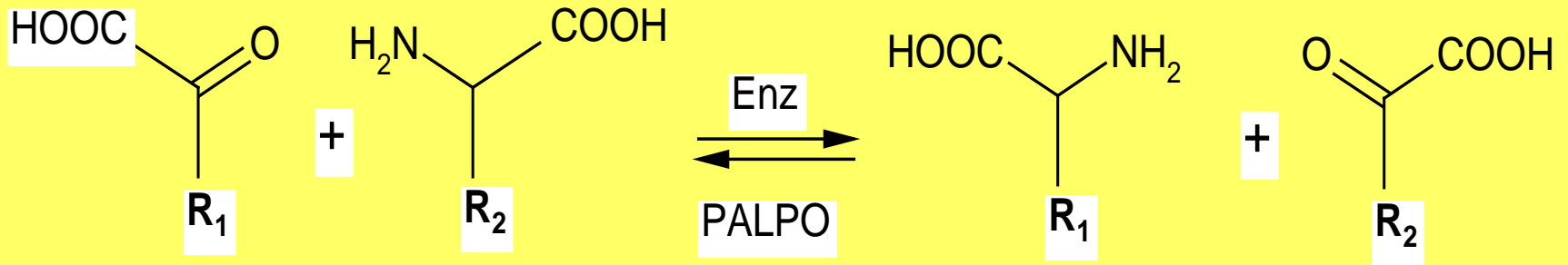
- glutamic acid and oxalacetic acid, SGOT
(from α -ketoglutaric acid and aspartic acid);
- glutamic acid and pyruvic acid, SGPT
(from α -ketoglutaric acid and alanine);

Now they are named for the substrates, the amino acids that react with α -ketoglutarate, as

- aspartate aminotransferase, AST, and
- alanine aminotransferase, ALT



"Transamination"

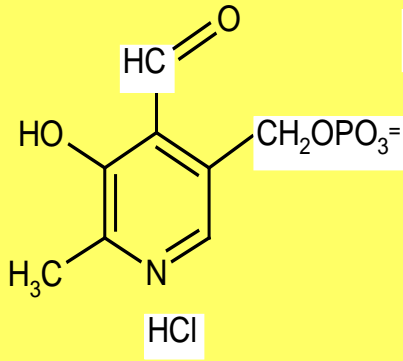


alpha-keto-
glutarate

aspartate
or
alanine

glutamate

oxalacetate
or
pyruvate




MD
or
LD

NADH
H⁺

malate
or
lactate



By removing the oxalacetic acid formed by transamination, reducing it to malic acid with added malic dehydrogenase and DPNH (NADH), the reaction was “pulled” rapidly to completion. It was easy to measure the NADH disappearance in a spectrophotometer at 340 nm, with results in just 5 minutes after about 10 minutes of stabilization.



As it chanced, the Professor of Pharmacology, Dr. Severo Ochoa heard the presentation and offered me a chance to work in his laboratory the following year. He allowed me to use his spectrophotometer, and provided useful advice. I had found that amino acids such as aspartate or alanine reacted with α -ketoglutarate to yield glutamine and oxalacetic or pyruvic acid, as a measure of the enzyme activities of SGOT or SGPT (now AST or ALT). I worked on a method to measure them by spectrophotometric disappearance of DPNH (NADH) as the keto acids were reduced.

TRANSAMINASE ACTIVITY IN HUMAN BLOOD

By ARTHUR KARMEN, FELIX WROBLESKI, AND JOHN S. LaDUE

(From the Sloan-Kettering Institute, Department of Medicine, Memorial Center, New York City, N.Y.)

(Submitted for publication April 3, 1954; accepted July 15, 1954)

TABLE V

Transaminase activity in blood of hospitalized patients in micromoles per ml per hr

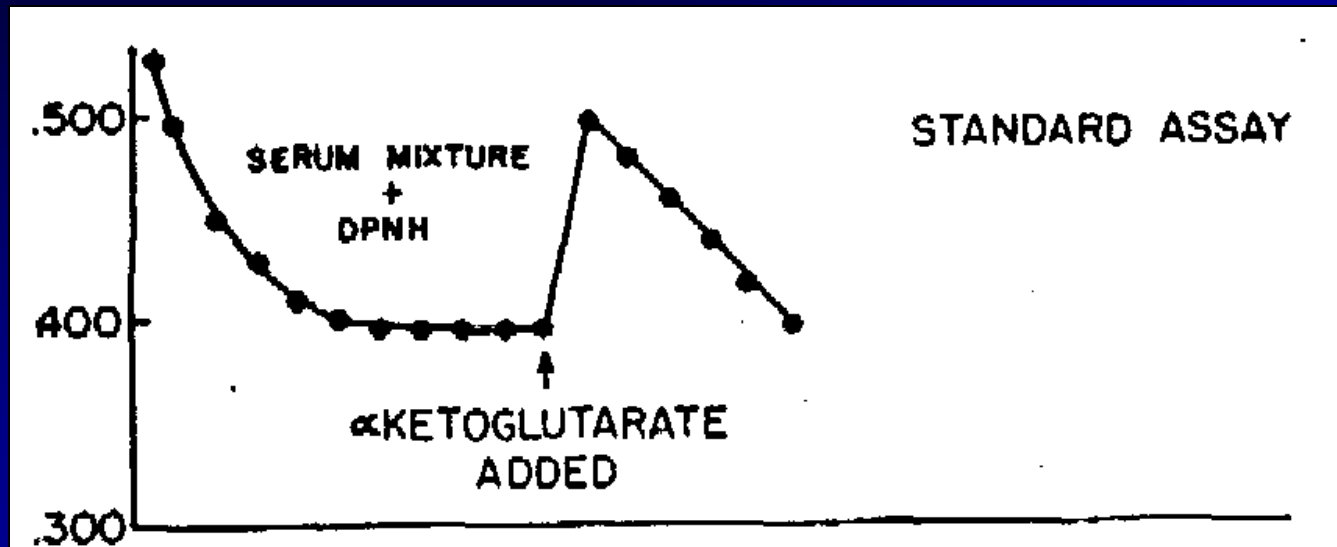
Clinical diagnosis	SGOT	SGPT	HGOT	HGPT
Carcinoma of lung	0.54	0.41	8.86	2.07
Lymphoma	0.74	0.53	6.35	2.00
Rhabdomyosarcoma	1.70	1.60	9.13	7.46
Acute hepatitis	1.97	1.75	7.20	10.40
Portal cirrhosis	0.49	0.38	3.10	1.40
Acute myocardial infarction	2.02	1.76		
Congestive heart failure	1.16	0.81	5.00	2.20

APPENDIX

A NOTE ON THE SPECTROPHOTOMETRIC ASSAY OF GLUTAMIC- OXALACETIC TRANSAMINASE IN HUMAN BLOOD SERUM


By ARTHUR KARMEN

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Severo Ochoa a few years later shared with Arthur Kornberg the Nobel Prize of 1959, for their work on describing the syntheses of RNA and DNA.



In one of my last papers published in 1997, I compared the use of SGOT (AST) with some newer biomarkers for cardiac injury that were more specific, and concluded that troponin (TnT) was much better.

Troponin-T as a Serum Marker for Myocardial Infarction

Vadiraja V. Murthy and Arthur Karmen

Albert Einstein College of Medicine, The Bronx, New York

J Clin Lab Anal. 1997; 11(3):125-8.

. . . but ALT has become the workhorse for assay of acute liver injury.



I went on to do an internship and medical residency at Bellevue Hospital and NYU, then to NIH for research on gas chromatography and lots of other projects. I did not get back to look again at transaminase for cardiac injury for a long while, but finally did so in 1997.