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50 Years Ago in *The Journal of Pediatrics*

The Diagnostic Value of Serum Enzyme Measurements

Howell, RR. J Pediatr 1966;68:121-34

Dr Howell reviews the (at that time) 36-year history of the value of serum enzymes in clinical practice. He traces the first diagnostic use of an enzyme, alkaline phosphatase (ALP), back to 1930. The methods used in 1966 were not standardized, and each enzyme had its own unit of measurement. The enzymes reviewed by Dr Howell are glutamic oxaloacetic and glutamic pyruvate transaminases, aldolase, creatine kinase, ALP, lactic dehydrogenase, acidic dehydrogenase, and amylase.

Now 50 years later almost all of these analytes are still in clinical use; some have changed names, and other biomarkers have been discovered. We no longer use transaminase levels to diagnose myocardial infarction, but aldolase and creatine kinase remain the serum markers for muscle disease. Today, we have more accurate and time saving equipment for analysis and standardization of measurement units across laboratories, but normal values continue to be reported differently.

Serum enzyme measurements play a crucial role in modern medicine now as they did in 1966, and we rely now on these markers more than ever. Dr Howell points out that vitamin B6 deficiency leads to low levels of transaminases. Low serum concentration of alanine transaminase has recently been shown to be predictive of all-cause mortality in adults.[1] ALP is an enzyme that normally is higher in growing children; however, this continues to raise questions among clinicians about the potential for underlying liver disease. The availability to fractionate bone and liver derived ALP enzyme helps solve this question. Low levels, however, could indicate zinc deficiency, which might be ignored as all of us are accustomed to looking for elevation as marker of disease.

Dr Howell's final comment remains true today: "there is no single change in serum enzyme which is absolutely specific for a given disease." We continue to aim for the development of a truly disease specific and sensitive biomarker. For children, this is especially needed as some of our diagnostic procedures may affect our patients in the long term (eg, the effect of general anesthesia on neurodevelopment).

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