

This Week's Citation Classic®

Boyd J W. The comparative activity of some enzymes in sheep, cattle and rats—normal serum and tissue levels and changes during experimental liver necrosis.

Res. Vet. Sci. 3:256-68, 1962.

[Biochemistry Dept., Agricultural Research Council, Inst. Animal Physiology, Babraham, Cambridge, England]

Certain enzymes (AST, ALT, GLDH, LDH, and ICDH) were assayed in tissues of sheep, cattle, and rats. Elevations of serum enzyme during toxic liver necrosis showed leakage of enzymes from damaged hepatocytes. The serum enzyme most affected was ALT in rats and GLDH in sheep and cattle. [The SCI® indicates that this paper has been cited in over 125 publications.]

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There were several laboratory tests available for the diagnosis of liver disease when I started work at the ARC Institute of Animal Physiology at Babraham near Cambridge in 1958. For example, serum alkaline phosphatase and bilirubin were moderately sensitive and specific tests of biliary obstruction, and serum albumin and dye excretion tests could detect severe losses of functional hepatic mass. However, there were no sensitive, specific tests for liver-cell damage.

My paper was among the first that combined the techniques of enzymology, histopathology, and induced liver necrosis to show the leakage of intracellular enzymes from damaged liver cells into plasma. Increased serum alanine aminotransferase (ALT) was liver specific in laboratory rats but not in farm animals. Increased serum glutamate dehydrogenase (GLDH) was a sensitive, specific test of liver damage in farm animals.

I think the great interest in this paper can be attributed to its publication when clinicians were seeking more sensitive diagnostic tests and many new drugs were being screened for their toxic side effects. This fundamental research contributed to the rapid expansion of serum enzymology as an important component in clinical pathology.

The subsequent mass production and distribution of test kits for diagnostic enzyme assays became a multimillion-dollar industry that facilitated serum enzyme testing in human and veterinary hospital laboratories. The development of automatic spectrophotometry enabled busy laboratories to assay serum enzymes more rapidly. When I was doing this research, slow manual spectrophotometers were used, and many hours of each day were spent patiently plotting enzyme reaction rates on graph paper using a pencil and a stopwatch.

This report was a forerunner to several others that led to the development of serum creatine kinase (CK) as a sensitive test for muscle disease in animals.¹ This expanded the number of organ-specific serum enzyme tests. The search for specificity was extended to the study of organ-specific isoenzymes. In particular, lactate dehydrogenase (LDH) was found to have important species-specific and organ-specific isoenzyme patterns.² I developed techniques for electrophoretic separation of isoenzymes and the visualization of isoenzymes by fluorescence or dye-binding. These rather colorful methods produced aesthetic as well as scientific satisfaction!

I have recently reviewed the current state of knowledge in the field of diagnostic enzymology in animal disease.³ My own contributions to this field were recognized in 1983 by the award of a Fellowship of the Royal College of Veterinary Surgeons in London.

1. Boyd J W. Creatine phosphokinase in normal sheep and in sheep with nutritional muscular dystrophy. *J. Comp. Pathol.* 86:23-8, 1976.
2. ———. Serum enzyme changes in lambs with experimentally-induced acute muscular dystrophy. *Res. Vet. Sci.* 5:419-33, 1964.
3. ———. The mechanisms relating to increases in plasma enzymes and isoenzymes in diseases of animals. *Vet. Clin. Pathol.* 12:9-24, 1983.