Molecular Basis of Pathogenesis in Parasitic Diseases. 2nd S-E Asian Symposium on Parasitology and Tropical Medicine Hong Kong 14-16/12/88

5. MITOCHONDRIAL ASPARTATE AMINOTRANSFERASE. SERUM LEVELS IN SCHISTOMOSIASIS JAPONICA

T.R.C. Boyde, Dept. of Biochemistry, University of Hong Kong. F. Monsanto, G. Ghislani (Tacloban), B. Blas, L. Tormis (Palo), Leyte, Philippines

There has been widespread concern about the lack of convenient measures of severity of liver involvement in cases of schistosomiasis. Following up old observations from Uganda and the present target area we have determined serum levels of the mitochondrial isoenzyme of aspartate aminotransferase (MAAT) in several groups of out- and in-patients at Palo.

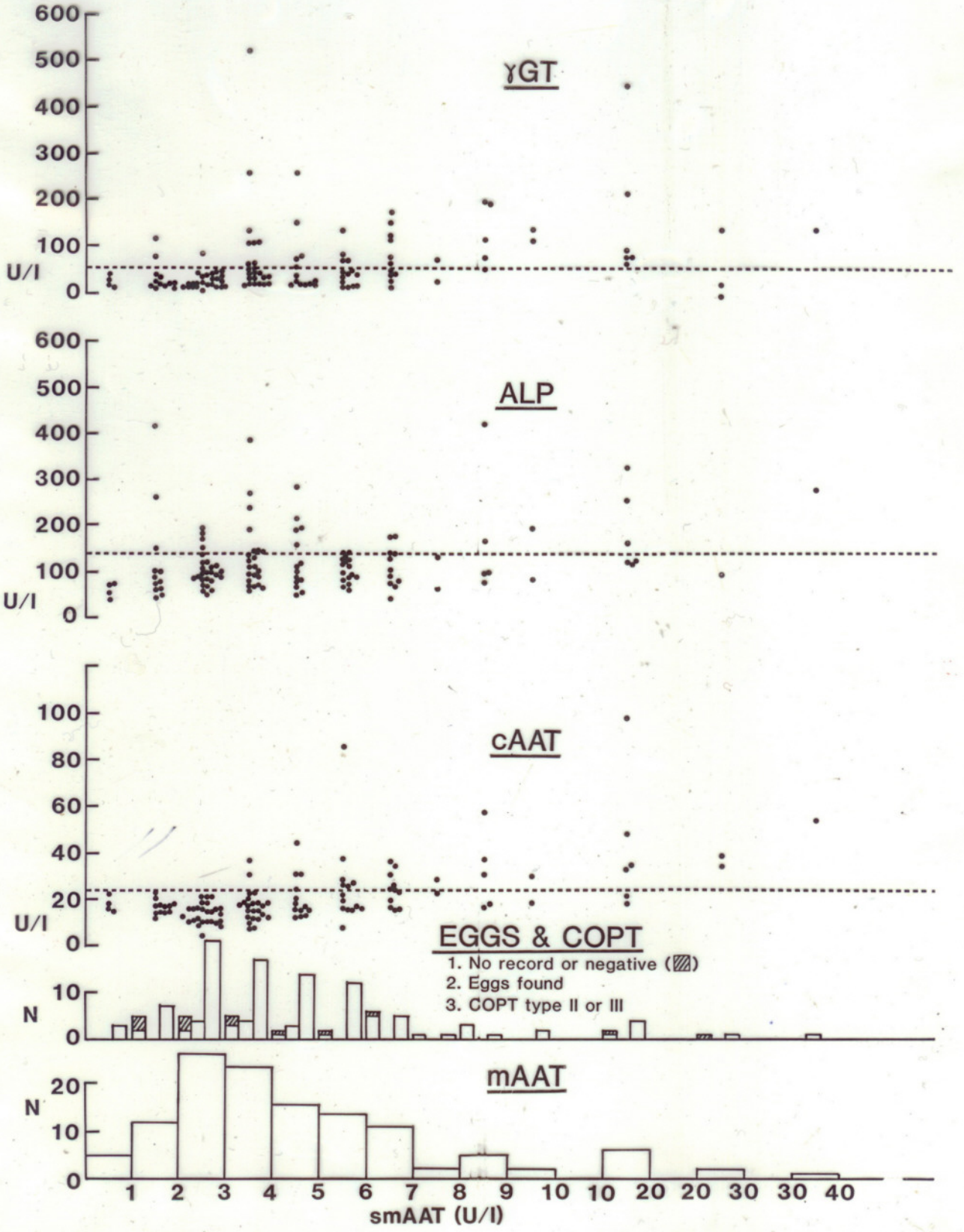
A province-wide programme of case-finding and treatment with praziquantel has operated for 5 years with manifest benefits on morbidity due to the parasite, and prevalence has halved. In these new circumstances, we found that most of the presenting patients (COPT- and/or egg-positive) had normal levels of both isoenzymes. However, a minority, which included the few with clinical evidence of liver involvement, had a raised level of MAAT either alone or proportionately more than the cytoplasmic izoenzyme. This pattern contracts sharply with that in viral or toxic hepatitis, and might reflect the liver pathology peculiar to schistosomiasis. Being relatively cheap and quick, the assay seems a worthy candidate for trial as an aid in case assessment.

For the avoidance of confusion:- Aspartate aminotransferase is the same as GOT, AspAT etc., but the isoenzymes are rarely measured separately and few methods can do this successfully. Alanine aminotransferase (GPT, AlAT, etc.) is a different enzyme. Few diseases affect MAAT levels specifically.

4. THE MOLECULAR MECHANISMS OF DRUG RESISTANCE IN GIARDIA

J.A. Upcroft, P.F.L. Boreham and P. Upcroft.
Queensland Institute of Medical Research, Bramston Terrace, Herston, Brisbane, 4006, Australia.

Treatment failures in Giardia intestinalis occur and drug resistance is responsible in many cases. Stocks of Giardia vary in their sensitivity to drugs both in vivo and in vitro. Organisms taken from patients who failed to respond to therapy with furazolidone were the least sensitive to the drug in axenic cultures. Resistance to metronidazole, a 5-nitroimidazole correlates with reduced levels of the enzyme pyruvate:ferredoxin oxidoreductase which reduces the drug to short lived, highly toxic intermediates. Nitrofuran (furazolidone) resistance correlates positively with concentrations of thiol cycling enzymes which defend the parasite against free radicals. Like Entamoeba histolytica, G. intestinalis has no endogenous glutathione but abundant quantities of other thiols. However, peroxidase and reductase activities which reduce exogenous glutathione are present. Cloned DNA probes for the different enzymes in the thiol cycling pathway can be used to study the prevalence, distribution and resurgence of drug resistant strains both at the level of chromosomal mutations, gene amplification and regulation. This approach can be used to assess the epidemiological implications of drug resistance, what proportion of treatment failures result from reinfection and the significance of animals as reservoirs of human Giardia infections.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EGGS & COPT
1. No record or negative (▨)
2. Eggs found
3. COPT type II or III
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