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Serum and Liver Transaminase Activities in Experimental Virus Heptatitis in Mice

An increase (20- to 40-fold) in the aspartic-ketoglutaric and alanine-ketoglutaric transaminase activities of the serum in human epidemic virus hepatitis was found by us (*1, 2*). Later, aspartic-ketoglutaric transaminase activity in epidemic hepatitis was investigated by Wróblewski and LaDue (*3*), and comparable results were obtained.

No such increase has been found in any other type of icteric or anicteric liver diseases that were investigated by Wróblewski and LaDue (*3*) and by us (*1, 2*), with the exception of myocardial (precocious) infarction (*4*). Furthermore, these authors found an increase in the aspartic-ketoglutaric transaminase activity of serum both in cases of carbon tetrachloride poisoning in human beings and in cases of experimental carbon tetrachloride poisoning in mice (*3*).

In epidemic hepatitis, the increase in alanine-ketoglutaric transaminase activity is more consistent than the increase in aspartic-ketoglutaric activity. Consequently, the ratio of aspartic-ketoglutaric transaminase activity to alanine-ketoglutaric transaminase activity (As-K/Al-K) falls from the normal (mean) value of 1.3 to 0.64 in acute epidemic hepatitis (*1, 2*). Such a pattern is retained by the serum of a patient during his convalescence, when the absolute values of the enzymatic activities of the patient's serum are no longer diagnostically significant. We have suggested that such enzymatic determinations could be of use as a diagnostic test for human epidemic hepatitis (*1*). Our later experiments (63 cases of epidemic hepatitis) fully confirm our first results (*5*).

Questions have arisen with regard to the following: (i) whether the increase of the enzymatic activities is really related to the destruction of parenchymal liver cells as suggested by us and others (*1–5*); (ii) whether such enzymatic variations are common features of all human (epidemic, yellow fever, infectious mononucleosis, and so on) and animal virus hepatitides; (iii) whether enzymatic variations that are observed in serums are associated with variations in the same activities in liver tissue; (iv) whether the possible enzymatic variations in liver tissue are analogous or opposite to those in serums from the same subjects.

The present results (Table 1) concern two enzymatic activities of the livers and serums of mice infected with 1000 LD_{50} of hepatitis virus (MHV-3 Craig, of Gledhill and Andrewes, *6*) and killed on the fourth day of the disease (*7*). Determinations were made according to Tonhazy, White, and Umbreit (*8*).

Determinations were made of enzymatic activity in homogenates of liver tissue from each of 15 infected mice and each of 15 normal mice and in five pools of serums from normal mice and five from infected mice. Each pool contained a mixture of serums from three animals. The results obtained led us to the following conclusions:

1) An increase is shown in the investigated transaminase activities in the serums of the animals experimentally infected with MHV-strain virus. This increase is comparable to that observed in human beings with epidemic hepatitis. Furthermore, the afore-mentioned decrease in the value of the As-K/Al-K ratio is found in the serum both in cases of human hepatitis and cases of experimental hepatitis in mice.

2) The variation in either of the transaminase activities in the liver (both decrease) of an animal is opposite to the variation in the analogous transaminase activity in the serum of the same animal but roughly proportional to the latter in magnitude. The decrease in the alanine-ketoglutaric transaminase activity in livers and the increase in this activity in serums are more pronounced than the changes in activities of aspartic-ketoglutaric transaminase in serums and livers.

These conclusions support the hypothesis that the enzymatic variations observed are not limited to human virus hepatitis (*9*). Furthermore, the necrosis of hepatic cells seems to play an important role in the pathogenesis of the phenomenon (passage from the liver to the blood of enzymatic metabolites).

FERNANDO DE RITIS
MARIO COLTORTI
GIUSEPPE GIUSTI
Istituto di Patologia Speciale, Medica e Metodologia Clinica, University of Naples, Italy

Table 1. Transaminase activities at 37°C of livers and serums of mice. Aspartic-ketoglutaric transaminase activity is measured in micromoles of oxalacetate formed, and alanine-ketoglutaric transaminase activity is measured in micromoles of pyruvate formed.

Item	Normal mice	Infected mice	± %	Student's *t*
*Liver**				
Oxalacetate	115.1	86.6	− 25	4.31†
Pyruvate	111.6	58.8	− 48	5.93†
As-K/Al-K	1.03	1.46	+ 41	3.70†
Serums‡				
Oxalacetate	2.98	31.7	+ 999	3.98§
Pyruvate	0.95	37.7	+3867	4.44§
As-K/Al-K	3.04	0.84	− 75	4.42§

* Averages of 15, 100 mg of tissue for 10 minutes. † t significant > 2.763 ($P = 0.01$), $G = 28$. ‡ Averages of five pools, each from three of the same mice, 1 ml for 15 minutes. § t significant > 3.355 ($P = 0.01$), $G = 8$.

References and Notes

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Consistent Biochemical Pattern in Malignant Tumors

In a previous study (*1*), a variety of normal and malignant tissues were subjected to cell fractionation by differential centrifugation. In all of the malignant tissues studied, the apportionment of protein among the various cell fractions showed a remarkably consistent pattern in which the nuclear and final supernatant-fluid fractions contained most of the protein and in which the mitochondrial and microsome fractions contained relatively little. The original series included 15 fractionations of nine malignant animal tumors, but only two human tumors.

Recently it has become possible to extend the observations to four more malignant human tumors (*2*). These included a lymph node affected by Hodgkin's disease, an inguinal lymph node containing an epidermoid carcinoma metastatic from the penis, a fibrosarcoma superficial to the posterior costal margin, and a cer-