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LRA by ELISA/ACT[®]

CLINICAL PEARLS UPDATE#13

Hepatitis

December 1, 2003

Dear Colleague:

Hepatitis (A, B, C, D, E...) and related syndromes (hepatidities) affect 15-39 million Americans according to the Liver Society and the Centers for Disease Control. Successful comprehensive management using LRA by ELISA/ACT[®] tests and treatment plans are illustrated in the attached abstract reports. Attached is a clinical update newsletter that details how this advanced approach can be applied in your practice with beneficial results.

Functional, *ex vivo* lymphocyte response assays (LRA by ELISA/ACT) offer the most advanced tests available for determination of the individual's responses to the widest available range of substances tested by any lab in the world.

We are grateful for the opportunities to be of service to you and your patients.

Sincerely,

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Lab Director

Jain SK, Pemberton PW, Smith A, McMahon RF, Burrows PC, Aboutwerat A, Warnes TW. Oxidative stress in chronic hepatitis C: not just a feature of late stage disease. *J Hepatol* 2002;36(6):805-811.

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BACKGROUND/AIMS: Chronic hepatitis C infection is a major world-wide problem, frequently progressing to cirrhosis, liver failure or hepatoma. The pathological mechanisms of disease progression are unclear but oxidant stress may play a role.

METHODS: Markers of lipid peroxidation, antioxidant status, hepatic fibrogenesis and liver function were measured in blood or urine from 42 chronic hepatitis C patients. Fibrosis was graded histologically in a subgroup of 33 patients.

RESULTS: The lipid peroxidation marker 8-isoprostane and the ratio of oxidized to reduced glutathione were significantly elevated ($P < 0.001$, $P = 0.006$). The antioxidants glutathione, selenium and vitamins A, C and E were significantly decreased (all $P < 0.001$) compared to age and sex matched controls. Abnormal values were more marked in cirrhotics, but significant changes were also observed in the non-cirrhotic group. The fibrosis score correlated positively with urinary 8-isoprostane and type III procollagen peptide and negatively with vitamin A.

CONCLUSIONS: Oxidant stress, as reflected in blood and urine by a wide range of pro- and antioxidant markers, is a significant feature of hepatitis C infection. Although more severe in the cirrhotic group, there was clear evidence of oxidant stress in non-cirrhotic patients. Antioxidant therapy may therefore have a role in slowing disease progression to cirrhosis.

On balance, what these studies show is that hepatitis is multifactorial. All of these components are included in the LRA by ELISA/ACT tests and treatment guide. Better outcomes are the results. Relief from the immune reactive oxidative stress by substituting for immunoreactive items plus patient specific antioxidant supplements and *The Alkaline Way* diet work together to reduce risk and enhance the chances of sustainable remission in people with hepatitis.

Farinati F, Cardin R, Degan P, De Maria N, Floyd RA, Van Thiel DH, Naccarato R. Oxidative DNA damage in circulating leukocytes occurs as an early event in chronic HCV infection. *Free Radic Biol Med* 1999;27(11-12):1284-1291.

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Chronic hepatitis C virus (HCV) infection is associated with an increased production of reactive oxygen species within the liver that are responsible for the oxidation of intracellular macromolecules. To ascertain whether the increased risk of hepatocellular carcinoma in individuals with chronic HCV infection is related to an accumulation of oxidative DNA damage, the 8-hydroxydeoxyguanosine (8-OHdG) content in the DNA of liver tissue and leukocytes of 87 individuals with HCV- or HBV-related liver disease and of 10 healthy controls was measured. Serum levels of thiobarbituric acid reactive substances (TBARS) were also assessed as an index of lipid peroxidation.



RESULTS: The 8-OHdG content in the circulating leukocytes correlated with that of liver tissue ($r = 0.618$, $p < .0004$). HCV patients had the highest median 8-OHdG levels ($p < .0004$). 8-OHdG leukocyte levels in HCV patients were higher than in HBV patients ($p < .04$) and they significantly correlated with the clinical diagnosis ($p < .025$), the serum ferritin levels ($p < .05$), and the amount of liver steatosis ($p < .001$). No correlation was found with age, gender, history of drinking or smoking, ALT or GGT levels, ESR, alpha-1, or gamma-globulin level and Ishak score. TBARS levels were significantly higher in cirrhotics than in noncirrhotics ($p < .01$).

CONCLUSIONS: The 8-OHdG level in circulating leukocytes is a reliable marker of oxidative stress occurring in the liver of individuals with chronic HCV infection. DNA oxidative damage appears to be an early and unique event in the natural history of HCV-related hepatitis. This injury increases the risk of genomic damage and may be one of the important factors involved in the carcinogenic process in cases of HCV-related chronic liver disease.

Note: We believe the comprehensive optional treatment guide included with LRA by ELISA/ACT tests, if requested, provides the best current therapy for sustained remissions in the hepatitises and related syndromes.

