



Functional Gastroenterology Bolus

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An Expanded View of Transaminases and New ACG Normal Values

Transaminase testing is common and included in most comprehensive metabolic panels. Over the last four decades, I have found that average healthy transaminase levels are in the high teens to the mid-twenty range, but I had no formal evidence for these being “ideal” values. Labs vary in their ranges for AST and ALT, but a common upper range of normal is 40-50 IU for males and slightly lower for females (Fried MW, 2008). Normal ranges are determined based on a “healthy” reference population. We now know that these “healthy” ranges are often found when testing people suffering from various degrees of chronic liver disease.

Reasons Why Chronic Liver Disease May Be Associated with Normal Transaminase Levels

Patients with chronic liver disease are often asymptomatic and may be diagnosed later in the course of these diseases. Examples include chronic active hepatitis C and non-alcoholic fatty liver disease both before and sometimes after progression to cirrhosis (Pratt DA, 2000 and Prati D, 2002). Recall also that transaminase levels may fluctuate between the high and normal range over time in patients with hepatitis C virus (HCV) due to spikes in viremia. Certain viral genotypes may be less likely to elevate the ALT level (Silini E, 1995 and Pontisso P, 1999). A less likely mechanism for this phenomenon would be a liver which is no longer able to release AST and ALT from hepatocytes. As the number of hepatocytes decreases with advanced cirrhosis, these serum markers become less reliable signs of hepatic disease.

Highest Incidence of Chronic Hepatitis C in Baby Boomers

The Centers for Disease Control recommends testing all baby boomers (born between 1945 and 1965) for hepatitis C virus (HCV) even if there is no other risk factor for HCV (www.cdc.gov/hepatitis/hcv/guidelinesc.htm). People in this age

group have the highest incidence of HCV hepatitis compared to any other cohort. As an explanation for high HCV rates in baby boomers, I suggest a theory:

- 1) The use of intranasal cocaine or injectable drugs of abuse was more casual in the 1960s and 1970s.
- 2) Boomers who used injection or non-injection drugs of abuse rarely, or even one time, may be reticent to admit that to their physician.
- 3) Boomers testing positive for HCV exposure may have a risk factor (non-injection cocaine use or injection of drugs of abuse) that is not divulged. There is weak epidemiological evidence for non-injection cocaine use and strong evidence for injection drug use associated with HCV transmission.

Research on Normal Range Serum Markers in Chronic Liver Disease

Multiple studies have uncovered evidence that transaminases need not be elevated in abnormal ranges to be indicators of liver disease. A study of 94,533 men and 47,522 women aged 35-59 years of age researched the predictive value of normal range liver function tests. This eight-year prospective study published in the *British Medical Journal*, showed that subjects with slightly increased transaminase levels, but still within the normal range, had higher risk for mortality from liver disease (Kim HC, 2004).

Fasting glucose, total cholesterol, and transaminases were tested yearly along with height, weight, and data on tobacco and alcohol use, family history, and any disease diagnoses. Outcomes employed were diagnosis of hepatic cancers or non-neoplastic hepatic diseases as listed on the death certificates of subjects who died during the study period. Only patients who had also been previously hospitalized for a liver-related diagnosis were included among those positive for chronic liver disease related deaths.

Adjusted relative risk of death from liver disease and slightly elevated (normal range) transaminases compared to levels less than 20 IU/L

	AST 20-29 IU/L	AST 30-39 IU/L	ALT 20-29 IU/L	ALT 30-39 IU/L
Men	2.5	8.0	2.9	9.5
Women	3.3	18.2	3.8	6.6

New American College of Gastroenterology Guidelines for Transaminases

Based on these findings and others, the American College of Gastroenterology (ACG) published new guidelines for transaminase normal ranges (Kwo PY, 2016). They state that a true healthy normal ALT level ranges from 29-33 IU/L for males and 19-25 IU/L for females. They recommend that higher levels should be assessed as signs of chronic liver disease.

Wang, et al found that higher, but within normal range ALT levels, independent of body mass index was a dose related predictor of type 2 diabetes in a Chinese population ($p < 0.001$, Wang CS, 2012). In a study of 7403 subjects, the upper limit for healthy range ALT level was deduced to be 31 IU/L for males and 23 IU/L for females. This study also found a higher prevalence of metabolic syndrome and insulin resistance with these higher, yet within normal range values (Kang HS, 2014).

Celiac Disease and Transaminases

Using traditional upper cutoff levels of 40 IU/L, chronic unexplained "transaminitis" has also been reported in about 40% of adult celiac patients compared to 0.5% of the general population (Bardella MT, 1999 and Rubio Tapia A, 2008). Always consider ordering screening serum tests for celiac disease (anti-gliadin antibody IgA and IgG, and/or anti-tissue transglutaminase IgA and IgG) when other causes of hepatic disease are not found in patients with elevated transaminases.

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